Division of Medicaid

Office of the Governor

State of Mississippi

DUR Board Meeting

February 21, 2008

2:00 p.m.

Woolfolk Building, Room 117

Jackson, MS

DIVISION OF MEDICAID
OFFICE OF THE GOVERNOR
DRUG UTILIZATION REVIEW BOARD
AGENDA

February 21, 2008

Welcome — **Frank Marascalco, RPh**

Old Business

- **Approval of Meeting Minutes**
- **Updates** — **Dennis Smith, RPh**
  - **Cost Management Analysis**

Pharmacy Program Update — **Judith Clark, RPh**

New Business — **Dennis Smith, RPh**

- **Overview of rDUR Process**
- **Utilization of Benzodiazepines, Carisoprodol, Hydrocodone, Ambien®, and Provigil® - Follow-up from November 2007 meeting**
- **Labeling Update for Desmopressin Acetate Nasal Spray**
- **Pharmacy Coverage of Tobacco Cessation Products**
- **Other Criteria Recommendations**
- **Boxed Warning Update**

Next Meeting Information — **Frank Marascalco, RPh**

Drug Utilization Review Board

Roy L. Arnold, Jr., R.Ph.
Clayton Drug Store
216 Main Street
Collins, MS 39428-0787
Term Expires: June 30, 2009

Harold B. Blakely, R.Ph.
Delta Area Hospice Care
5357 Cliff Gookin Boulevard
Tupelo, MS 38801
Term Expires: June 30, 2008

Laura Gray, M.D.
905 Garfield Street
Tupelo, MS 38801
Term Expires: June 30, 2008

John M. Wallace, M.D.
Jefferson Medical Clinic
1203 Jefferson Street
Laurel, MS 39440
Term Expires: June 30, 2009

Frank Marascalco, R.Ph
Sav-Mor Drugs
1967 Commerce Street
Grenada, MS 38901
Term Expires: June 30, 2008

Wallace Strickland
Rush Foundation Hospital
8219 Sycamore Creek Drive
Meridian, MS 39305
Term Expires: June 30, 2008

Lee Voulters, M.D.
1340 Broad Ave Suite 440
Gulfport, MS 39501
Term Expires: June 30, 2009

Upcoming Mississippi DUR Board Meeting Dates

May 15, 2008
August 21, 2008
November 20, 2008
February 19, 2009

Mississippi Division of Medicaid
Drug Utilization Review (DUR) Board
Minutes of the November 15, 2007 Meeting

Members Attending: Billy Brown, PharmD.; Randy Calvert, R.Ph., Laura Gray, M.D.; Frank Marascalco, R.Ph., Chair; Andrea Phillips, M.D.; Lee Voulters, M.D.; Wallace Strickland

Members Absent: Roy Arnold, R.Ph.; Harold Blakely, R.Ph.; John Wallace, M.D.

Also Present:
DOM Staff: Judith Clark, R.Ph., DOM Pharmacy Bureau Director; Paige Clayton, PharmD, DOM DUR Coordinator; Carlis Faler, DOM Program Integrity Director

HID Staff: Dennis Smith, R.Ph., Project Manager; Ashleigh Holeman, PharmD; Kathleen Burns, R.N.

Call to Order:
Frank Marascalco, Chairman of the Board, called the meeting to order at 2:10 p.m.

Dr. Clayton asked that the Board proceed with business not requiring a vote while awaiting arrival of enough members to constitute a quorum.

Updates:
Cost Management Analysis
Mr. Smith began by presenting reports reflecting several months of data. Antipsychotic agents continued to lead the top 15 therapeutic classes by total cost of claims throughout the five month period reported. The top drugs based on number of claims were led by hydrocodone-acetaminophen and followed by Zyrtec. Dr. Holeman added that the top 200 national ranking for each drug has been added to the report for reference. This report also designates by an asterisk those products classified as preferred on the preferred drug list. These additions were made to facilitate the understanding of the number of claims for these top medications. The top drugs based on total claims cost were led by Singulair® in April 2007. At this time, Mr. Smith and Dr. Holeman reviewed the findings of the analysis of Singulair® utilization that was presented during the previous DUR Board meeting. Of 4,500 patients not having a diagnosis of either asthma or allergic rhinitis, the majority were found to have had a non-specific upper respiratory diagnosis. The report further found that from May 2006 to May 2007, approximately 62 percent of patients receiving Singulair® had an asthma diagnosis, while approximately 65 percent of patients who received Singulair® had an allergic rhinitis diagnosis. According to this information, there did not appear to be gross over utilization of Singulair®. The Board agreed with these findings. Dr. Holeman continued with the top 25 drugs based on total claims cost by pointing out the remaining four months was led by Risperdal®.

Old Business:

Due to the lack of a quorum at the September 20, 2007 meeting, Mr. Smith briefly summarized several reports that were presented during the meeting.

Potential Misuse of ADHD Agents

The first of these reports was a review of the utilization of stimulants indicated for the treatment of ADHD. Although the study findings did not indicate extensive over-prescription of these agents among adults, a retrospective DUR criterion was recommended to identify adult patients who may be using these medications inappropriately. After discussion, Mr. Strickland made a motion to approve the criterion and Dr. Phillips offered a second. The motion was unanimously approved.

Inappropriate Use of Antibiotics

Mr. Smith next introduced the report which focused on the possible negative impact of the over-prescription of antibiotics to very young children. He reiterated that the Board had reached a consensus during the September meeting to not address this issue from a retrospective DUR perspective at this time.

HIV Criteria Report

Dr. Holeman presented a synopsis of the retrospective DUR activity that has resulted from the DUR Board's approval in May of a large group of criteria focusing on the encouragement of appropriate antiretroviral therapy. A focused inquiry into the severity of the exceptions generated in May and June revealed that there is not a significant drug therapy problem in HIV patients enrolled in Mississippi Medicaid. Dr. Holeman continued that since the appropriate use of HIV medications is imperative for each patient, retrospective DUR criteria will continue to be used to assist physicians in providing effective treatment for their HIV patients.

New Business:

Alprazolam and Lorazepam Utilization

Due to a high number of claims for alprazolam and lorazepam and at the request of the board during the September meeting, Mr. Smith presented a review of the utilization of these agents. Due to their anxiolytic effects, these medications tend to have a very high abuse potential. The results of this review were somewhat surprising in that the highest utilization occurred among beneficiaries in the 30 to 59 age range. Utilization was also determined in the long-term care population and found that there were a relatively small number of claims in this group. It was noted that while Medicare Part D provides the majority of drug coverage for dually-eligible patients, coverage of generic benzodiazepines such as alprazolam and lorazepam falls through to Medicaid. The board members recommended further study of this utilization by HID with the removal of the one time fills for all groups. Dr. Voulters also requested that HID review chronic users such as those with two or more refills. Dr. Gray suggested that HID identify patients on concurrent SSRI therapy. Mr. Strickland pointed out that, with the new wavier program allowing patients to receive long term care at home from a relative, this data might be skewed. It was suggested that HID include plan number and category of eligibility when the reports are re-run. Dr Voulters also requested that HID look at the long-acting benzodiazepines focusing on the LTC and elderly groups. Dr. Phillips continued with a

request to add diazepam to the review as she is seeing it used more frequently in her practice with patients requesting refills from other physicians. Carlis Faler, Program Integrity Director, added that it may be helpful for these reports to also reflect gender.

Hydrocodone Utilization
Hydrocodone remains consistently one of the top five drugs based on the number of claims. This has generated a concern with the DUR Board as to how Medicaid can address this over -utilization with its beneficiaries. While high rates of hydrocodone use are cause for concern both at the state and national level, it is difficult to identify the complexity of the problem as Medicaid has set a monthly dispensing limit of 62, or two doses per day per running 31 days. It was noted that in some cases, beneficiaries are paying cash for the remainder of the prescription. Medicaid is working with the State Pharmacy Board to gain access to available data on cash purchases by Medicaid beneficiaries. This is expected to add valuable input into the possible abuse of these products and other medications of interest. Dr. Voulters requested an age analysis be generated as was done on the benzodiazepines. In addition, he further requested that other medications with abuse potential have the same detailed reports run. Dr. Gray requested that HID continue to review carisoprodol and run a comparison on all three of these medications with their age, diagnosis and long term utilization. She also suggested that HID report on the effectiveness of the carisoprodol Medicaid Prescribing Update, or "one-pager" that was previously approved by the DUR Board.

Impact of Quinine Removal on Utilization of Gabapentin and Lyrica®
Dr. Holeman presented a review of the impact of FDA action in removing quinine products from the market. On December 11, 2006, the FDA ordered all manufacturers to stop marketing unapproved products containing quinine. Currently, Qualaquin® is the only FDA approved product that contains quinine. Quinine is approved for the treatment of malaria but is often used off-label for leg cramps. Because of the drug's risks, FDA believes that it should not be used to prevent and treat leg cramps. At the request of the DUR Board, utilization data was gathered by HID on the continued use of quinine after the FDA mandate. The searches performed by HID were for utilization of quinine, gabapentin and Lyrica® and attempted to identify trends based on the date that firms had to cease marketing quinine, February 13, 2007. While some increase was noted in utilization of gabapentin and Lyrica®, it was not as large as expected. HID generated a second chart reflecting the use of Requip® and Mirapex ® which are indicated for restless leg syndrome and concluded that physicians are possibly utilizing these medications in place of quinine products. The data presented was interpreted to indicate that appropriate therapy has generally been implemented by treating physicians in the wake of the change in the marketplace.

Duplicate Utilization of Risperdal Consta® and Oral Atypical Antipsychotic Agents
Mr. Smith next presented a review of the utilization of Risperdal Consta®, a long-acting atypical antipsychotic injection approved for the treatment of schizophrenia. This agent is well-suited for patients for whom medication compliance is a challenge. According to the FDA-approved prescribing information, tolerability to oral Risperdal® should be established prior to initiating therapy with Risperdal Consta®. The labeling also stated

that oral risperidone or another antipsychotic medication should be given with the first injection of Risperdal Consta®, continued for three weeks, then discontinued to ensure that effective therapeutic plasma concentrations are reached and maintained prior to the main release phase of risperidone from the injection site. Mr. Smith continued by presenting findings of searches made by HID of the utilization from 1/1/2007 through 09/21/2007. The beneficiaries identified in these searches were intersected to determine those with utilization of Risperdal Consta® and one or more oral atypical antipsychotic agents. Beneficiaries with claims totaling less than 32 days of treatment with an oral agent were excluded from the study. The search resulted in 191 beneficiaries who received long-acting injectable risperidone and oral atypical antipsychotic therapy during the time period searched. According to this analysis, over 50 percent of the beneficiaries on Risperdal Consta® received greater than 31days of treatment with an oral atypical antipsychotic during the reviewed time. These findings indicate that many beneficiaries are receiving duplicate atypical antipsychotic treatment in addition to Risperdal Consta®. As a result, a retrospective DUR criterion was recommended to alert prescribers to the appropriate prescribing guidelines for this product. HID will bring such a criteria before the DUR Board at the next meeting for review and approval.

Approval of Minutes

Dr. Phillips voiced the need to be excused and requested that voting on appropriate matters take place due to the fact that when she left there would no longer be a quorum. The minutes of the previous two DUR board meetings on May 19, 2007 and September 20, 2007 were approved with a motion by Mr. Strickland and a second from Dr. Phillips. All members voted in favor of the motion.

Fourth Quarter Criteria Recommendations

In order to allow for voting on retrospective criteria recommendations, Mr. Smith presented the following criteria to the Board for approval.

- Elidel or Protopic/ Therapeutic Appropriateness - The topical calcineurin inhibitor, Elidel (pimecrolimus) or Protopic (tacrolimus), is indicated as second-line therapy for the short-term, non-continuous chronic treatment of mild to moderate atopic dermatitis in patients who are unresponsive or intolerant to other agents. Rare cases of malignancy (i.e., skin cancer and lymphoma) have been reported in patients treated with topical pimecrolimus. Application should be limited to the areas affected with atopic dermatitis.
- Protopic or Elidel / Age Appropriateness - The topical calcineurin inhibitors, Protopic (tacrolimus) and Elidel (pimecrolimus), are not recommended for use in children less than 2 years of age. The long-term safety and effects of these agents on the developing immune system are unknown.
- Protopic 0.1% / Age Appropriateness - The use of Protopic 0.1% ointment (topical tacrolimus) is not recommended in children less than 15 years of age. The 0.03% tacrolimus ointment is approved for use in children ages 2 to 15. Application should be limited to areas affected with atopic dermatitis. If signs and symptoms have not resolved within 6 weeks patient should be re-examined to confirm diagnosis.

- Elidel or Protopic/ Immunocompromised Patients - Elidel (topical pimecrolimus) or Protopic (topical tacrolimus) should not be used in immunocompromised adults and children. These patients are at risk for increased systemic exposure and adverse effects of pimecrolimus or tacrolimus.
- Topical Immunomodulators / Therapeutic Duplication - Therapeutic duplication of topical immunomodulator agents may be occurring.
- Tizanidine / Ciprofloxacin - Concurrent use of tizanidine and ciprofloxacin, a potent CYP 1A2 inhibitor, is contraindicated. Co-administration of these agents has been shown to cause significant increases in the AUC and Cmax of tizanidine resulting in hypotension, excessive sedation, and psychomotor impairment.
- Tizanidine / Fluvoxamine - Concurrent use of tizanidine and fluvoxamine, a potent CYP 1A2 inhibitor, is contraindicated. Significant alterations of pharmacokinetic parameters of tizanidine, including AUC, t1/2, Cmax, increased oral bioavailability and decreased plasma clearance, have been observed with concomitant fluvoxamine administration. Coadministration of these agents has resulted in profound hypotension, bradycardia and excessive drowsiness.
- Pioglitazone / Therapeutic Appropriateness - Pioglitazone-containing products (Actos/ActoPlusMet/Duetact) may increase the risk of fractures in female patients. Analysis of clinical trial data revealed an increased incidence of fractures in female patients taking long-term pioglitazone therapy as compared to females taking a comparator (placebo or active). Consider the risk of fractures when initiating or treating female, type 2 diabetic patients with pioglitazone.
- Rosiglitazone or pioglitazone/ Congestive Heart Failure & Fluid Retention – Rosiglitazone or pioglitazone-containing products may cause or exacerbate congestive heart failure. Their use is contraindicated in patients with NYHA class 3 or 4 heart failure and not recommended in patients with symptomatic heart failure. Patients should be observed for signs and symptoms of heart failure (rapid weight gain, dyspnea, and /or edema). If heart failure develops initiate appropriate therapy and consider alternative antidiabetic therapy.
- Codeine / Pregnancy - Nursing infants may be at an increased risk of morphine overdose if their mothers are taking codeine-containing products and are ultra-rapid metabolizers of codeine. If codeine use is necessary in the nursing mothers prescribe the lowest effective dose for the shortest amount of time. Inform mothers receiving codeine of the potential risks and signs of morphine overdose in themselves and their infants.
- Stimulants / Therapeutic Duplication - Therapeutic duplication of stimulants may be occurring (methylphenidate, dexmethylphenidate, amphetamine mixtures, methamphetamine, dextroamphetamine, lisdexamfetamine).
- Immediate Release Stimulants / Drug Abuse / Negating Agents - The patient has a diagnosis of substance use disorder (SUD) and is receiving immediate-release stimulant medication. Treatment recommendations for patients with the dual diagnosis of ADHD and SUD suggest that ADHD be treated with non-stimulant agents, extended-release stimulants or transdermal stimulant formulations to reduce the potential for misuse, abuse and/or diversion.

- Amphetamines / History of Drug Abuse - Amphetamines are contraindicated in patients with a history of drug abuse. Chronic, abusive use can lead to tolerance, extreme psychological dependence, and severe social disability.
- Stimulants / Arrhythmias & Cardiac Conditions - Stimulant products generally should not be used in children or adolescents with known structural cardiac abnormalities, cardiomyopathy, serious rhythm abnormalities or other serious cardiac problems. Sudden death has been reported in association with CNS stimulant treatment at usual doses in this population. All patients treated with stimulant medications should have a careful history (including family history of sudden death or ventricular arrhythmia) and physical exam to assess presence of cardiac disease.
- Stimulants /Bipolar Disorder - Particular care should be taken when using stimulants to treat ADHD patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder, and such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder and depression.
- Selzentry / Nonadherence - A review of the patient's prescription refill history suggests that the patient may not be taking the drug in the manner it was prescribed. Non-adherence to antiretroviral therapy may result in insufficient drug plasma levels and partial suppression of viral load leading to the development of resistance, HIV progression, and increased mortality.
- Selzentry /Therapeutic Appropriateness - Selzentry (maraviroc) is FDA approved to be used in combination with other antiretroviral agents to treat adult patients infected with only CCR5-tropic HIV-1 detectable virus, who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents. There is insufficient data to recommend monotherapy with this agent.
- Selzentry /Cardiovascular Events - Selzentry (maraviroc) should be used with caution in patients at increased risk for cardiovascular events. In clinical studies, more cardiovascular events, including myocardial ischemia and/or infarction, were observed in patients who received maraviroc as compared to placebo (1.3% vs. 0%).
- Selzentry /Liver Impairment - Selzentry (maraviroc) has been linked to hepatotoxicity that may be preceded by a systemic allergic reaction (e.g., pruritic rash, eosinophilia, or elevated IgE). Discontinuation of maraviroc should be considered in any patient with signs and symptoms of hepatitis, or with increased liver transaminases combined with rash or other systemic symptoms. Caution is advised if maraviroc is used in patients with pre-existing liver dysfunction or who are co-infected with hepatitis B or C.
- Selzentry / High Dose - The recommended dose of Selzentry (maraviroc) for patients receiving concomitant therapy with NRTIs, tipranavir/ritonavir, nevirapine, and other drugs that are not strong CYP3A inhibitors or CYP3A inducers is 300 mg twice daily.
- Selzentry / High Dose - Selzentry (maraviroc) is metabolized by the CYP3A isoenzyme and patients receiving concomitant therapy with protease inhibitors

(except tipranavir/ritonavir), delavirdine, ketoconazole, itraconazole, clarithromycin, or other strong CYP3A inhibitors (e.g., nefazodone and telithromycin) should receive a reduced dose of 150 mg of maraviroc twice daily.

- Selzentry / Low Dose - Selzentry (maraviroc) is metabolized by the CYP3A isoenzyme and patients receiving concomitant treatment with CYP3A inducers (e.g., efavirenz, rifampin, carbamazepine, phenobarbital, and phenytoin), without a strong inhibitor, should receive a dose of 600 mg of maraviroc twice daily.
- Selzentry / Renal Impairment - Selzentry (maraviroc) should be used with caution in patients with renal impairment, particularly in those with concurrent use of a CYP3A inhibitor and a CrCl < 50 mg/mL. Approximately 25% of maraviroc is renally eliminated and impairment may lead to increased drug concentrations and risk of dose-related adverse effects (e.g., dizziness and postural hypotension). Patients should be monitored for adverse effects.
- Selzentry / Hypotension - Selzentry (maraviroc) should be used with caution in patients with a history of postural hypotension or who are on concomitant medication known to lower blood pressure. The frequency of postural hypotension is increased at higher than recommended doses of maraviroc.
- Selzentry /Therapeutic Appropriateness - Selzentry (maraviroc) should only be used in combination with other antiretroviral agents in adult treatment-experienced patients infected with CCR5-tropic HIV-1 detectable virus, who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents. The agent is not active against CXCR4-tropic and dual-tropic viruses. Tropism testing and treatment history should guide use of maraviroc.
- Viracept / Therapeutic Appropriateness - Viracept (nelfinavir) has been found to contain the process-related impurity ethyl methanesulfonate (EMS), a potential human carcinogen. The FDA states that pediatric patients stable on nelfinavir therapy may continue therapy due to a favorable benefit-risk ratio. Pediatric patients who need to begin HIV treatment should not start on a regimen containing nelfinavir until further notice.
- Viracept / Therapeutic Appropriateness - Viracept (nelfinavir) has been found to contain the process-related impurity ethyl methanesulfonate (EMS), a potential human carcinogen. The FDA has recommended that pregnant patients currently receiving nelfinavir be switched to an alternative agent if possible and that those needing to begin HIV treatment not be offered nelfinavir until further notice. Pregnant women with no alternative treatment options may continue to receive nelfinavir because the benefit-risk ratio remains favorable.
- Haloperidol / Therapeutic Appropriateness - Higher doses and intravenous administration of haloperidol appear to be associated with an increased risk of QT prolongation, torsades de pointes and even sudden death. Particular caution is advised when prescribing haloperidol to patients with predisposing factors (e.g., cardiac abnormalities, hypothyroidism and electrolyte imbalance) that could cause an even greater risk of these serious adverse effects.
- Haloperidol / Over utilization - Haloperidol may be over-utilized. The recommended maximum dose is 100 mg per day. Exceeding this dose may enhance the risk of adverse effects (e.g., QT prolongation, torsades de pointes, extrapyramidal symptoms, seizures, and hypertension).

- Fentora / Therapeutic Appropriateness - Fentora (buccal fentanyl) is only approved for the treatment of breakthrough pain in patients with cancer who are already receiving and are tolerant to opioid therapy. Buccal fentanyl must not be used in opioid non-tolerant patients. The improper selection of patients, incorrect dosing and improper product substitution may result in a fatal overdose with this agent.
- Quetiapine / Substance Abuse - Seroquel (quetiapine) should be prescribed with caution to patients with a history of substance abuse. The agent has sedative and anxiolytic properties and may be misused by some patients. Closely observe patients for signs of misuse or abuse (e.g., development of tolerance, increases in dose, drug-seeking behavior). Inappropriate use of quetiapine may put patients at risk for arrhythmias, hypotension, weight gain, and diabetes.

Mr. Marascalco continued with a vote on the criteria presented by HID. Dr. Phillips made a motion to approve the criteria presented with the exceptions of the pioglitazone/therapeutic appropriateness criteria and the pioglitazone/congestive heart failure and fluid retention criteria. Dr. Gray seconded the motion and all voted in favor.

Appropriate Antibiotic Use

Dr. Holeman presented a review of the appropriate utilization of antibiotics by Medicaid prescribers. Antimicrobial resistance among pathogens has become a common clinical problem and the association of resistance with the use of antimicrobial drugs has been documented in both inpatient and outpatient settings. This seems to have been given credence by the spread of organisms, such as MRSA, all essentially untreatable with routinely available antibiotics. Dr. Holeman continued by stating that decreasing the inappropriate use of antimicrobials has been listed as a primary solution to address the threat that antimicrobial resistance poses. To help combat the risk, HID presented and recommended the use of a Medicaid Prescribing Information Update, or "one-pager", which outlines the importance of appropriate treatment of upper respiratory tract infections and of prudent prescribing of antibiotics. HID recommends distribution of this document to prescribers by the Academic Detailing Staff and availability from the Division of Medicaid's website. After discussion of this approach, the Board's consensus was to support the distribution of this information as recommended.

Dr. Holeman then addressed the use of Zyvox®. At present, this antibiotic is non-preferred and subject to manual prior authorization review. Several recent studies have shown that outpatient use of Zyvox® may lower costs and prevent or shorten hospitalizations. Dr. Brown asked about the turn-around time of the prior authorization process. Mr. Smith answered that DOM requires that requests be processed within 24 hours, although most are responded to in less time. After discussion, the clear consensus of the DUR Board was to recommend no change to the present status of this product, continuing to require prior authorization approval, while encouraging appropriate use of this product.

Other

Dr. Gray suggested that HID analyze the utilization trends of Provigil® for the next Board meeting.

Boxed Warnings Update
Mr. Smith presented black box warnings, other warnings, and labeling changes issued by the FDA concerning the following:

Avandia (rosiglitazone)
FDA informed healthcare professionals of a potential safety issue related to Avandia (rosiglitazone). An on-going analysis of safety data for the treatment of type 2 diabetes mellitus using Avandia showed differing rates of ischemic cardiovascular events including heart attack or heart-related adverse events, some fatal, relative to other drugs used to treat diabetes mellitus. The clinical studies reviewed to date vary with respect to their populations, treatment regimens, and length of follow-up. Based on these data, the risk of ischemic cardiovascular events due to Avandia remain unclear. Prescribers should continue to carefully make individualized treatment decisions for patients with diabetes mellitus.

Exjade (deferasirox) Tablets For Oral Suspension
Novartis and FDA notified healthcare professionals of changes to the WARNINGS and ADVERSE REACTIONS sections of the product labeling for Exjade, a drug used to treat chronic iron overload due to blood transfusions (transfusional hemosiderosis) in patients 2 years of age and older. Cases of acute renal failure, some with a fatal outcome, have been reported following the post marketing use of Exjade. Most of the fatalities occurred in patients with multiple co-morbidities and who were in advanced stages of their hematological disorders. Additionally, there were post marketing reports of cytopenias, including agranulocytosis, neutropenia and thrombocytopenia in patients treated with Exjade where some of the patients died. The relationship of these episodes to treatment with Exjade is uncertain. Most of these patients had preexisting hematologic disorders that are frequently associated with bone marrow failure. Further, cases of leukocytoclastic vasculitis, urticaria, and hypersensitivity reactions (including anaphylaxis and angioedema) were reported. Healthcare professionals should monitor serum creatinine in patients who are at increased risk of complications, having preexisting renal conditions, are elderly, have co-morbid conditions, or are receiving medicinal products that depress renal function. Blood counts should also be monitored regularly and treatment should be interrupted in patients who develop unexplained cytopenia.

Propofol (marketed as Diprivan and generic products)
FDA informed healthcare professionals about several clusters of patients who experienced chills, fever, and body aches shortly after receiving propofol for sedation or general anesthesia. Multiple vials and several lots of propofol used in patients who experienced these symptoms were tested and there was no evidence that the propofol vials or prefilled syringes used were contaminated with bacteria or endotoxins. Propofol is an intravenous sedative-hypnotic agent for use in the induction and maintenance of anesthesia or sedation. To minimize the potential for bacterial contamination, propofol

vials and prefilled syringes should be used within six hours of opening and one vial should be used for one patient only. Patients who develop fever, chills, body aches or other symptoms of acute febrile reactions shortly after receiving propofol should be evaluated for bacterial sepsis. Healthcare professionals who administer propofol for sedation or general anesthesia should carefully follow the recommendations for handling and use in the product's full prescribing information.

Rocephin (ceftriaxone sodium) for Injection
Roche and FDA informed healthcare professionals of revisions to the CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION sections of the prescribing information for Rocephin for Injection. The revisions are based on new information that describes the potential risk associated with concomitant use of Rocephin with calcium or calcium containing solutions or products. Cases of fatal reactions with calcium-ceftriaxone precipitates in the lungs and kidneys in both term and premature neonates were reported. Hyperbilirubinemic neonates, especially prematures, should not be treated with Rocephin. The drug must not be mixed or administered simultaneously with calcium-containing solutions or products, even via different infusion lines. Additionally, calcium-containing solutions or products must not be administered within 48-hours of the last administration of ceftriaxone.

Use of CellCept (mycophenolate mofetil) associated with increased pregnancy loss and congenital malformations
Roche and FDA notified healthcare providers that use of CellCept (mycophenolate mofetil) is associated with increased risk of first trimester pregnancy loss and increased risk of congenital malformations, especially external ear and facial abnormalities including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney.
Based on postmarketing data from the United States National Transplantation Pregnancy Registry and additional postmarketing data collected in women exposed to systemic mycophenolate mofetil during pregnancy, the pregnancy category for CellCept has been changed from Category C (risk of fetal harm cannot be ruled out) to Category D (positive evidence of fetal risk). Labeling changes include the following sections: BOXED WARNING, WARNINGS/Pregnancy and Pregnancy Exposure Prevention, PRECAUTIONS/Information for Patients, and ADVERSE REACTIONS/Postmarketing Experience.

Within one week of beginning CellCept therapy, women of childbearing potential should have a negative serum or urine pregnancy test. In addition, women of childbearing potential (including pubertal girls and peri-menopausal woman) taking CellCept must receive contraceptive counseling and use effective contraception. Healthcare professionals and patients should be aware that CellCept reduces blood levels of the hormones in the oral contraceptive pill and could theoretically reduce its effectiveness. See the Dear Healthcare Professional Letter for additional recommendations for women of childbearing potential.

Provigil (modafinil) Tablets- WARNINGS Added To Prescribing Information Regarding Serious Rash And Hypersensitivity Reactions, And Psychiatric Symptoms

FDA and Cephalon notified healthcare professionals of Warnings added to prescribing information for Provigil (modafinil). Provigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder. The revised prescribing information updates safety information to include warnings regarding serious rash, including Stevens-Johnson Syndrome (SJS) and hypersensitivity reactions, and psychiatric symptoms. Rare cases of serious or life-threatening rash, including Toxic Epidermal Necrolysis, and Drug Rash with Eosinophilia and Systemic Symptoms have been reported in adults and children in worldwide postmarketing experience. Angioedema and multi-organ hypersensitivity reactions have also been reported in postmarketing experience.

Physicians should instruct their patients to immediately discontinue the use of Provigil and contact them if a rash or other hypersensitivity reaction occurs. Healthcare professionals and consumers should also be aware that Provigil is not approved for use in pediatric patients for any indication. In addition, psychiatric adverse experiences (including anxiety, mania, hallucinations, and suicidal ideation) have been reported in patients treated with Provigil. Caution should be exercised when Provigil is given to patients with a history of psychosis, depression, or mania.

Additional labeling revisions were made to the CLINICAL PHARMACOLOGY, PRECAUTIONS, and PATIENT PACKAGE INSERT sections.

Byetta (exenatide) and postmarketing reports of acute pancreatitis

FDA has reviewed 30 postmarketing reports of acute pancreatitis in patients taking Byetta (exenatide), a drug used to treat adults with type 2 diabetes. An association between Byetta and acute pancreatitis is suspected in some of these cases. Amylin Pharmaceuticals, Inc. has agreed to include information about acute pancreatitis in the PRECAUTIONS section of the product label.

Healthcare professionals should be alert to the signs and symptoms of acute pancreatitis and instruct patients taking Byetta to seek prompt medical care if they experience unexplained, persistent, severe abdominal pain which may or may not be accompanied by vomiting. If pancreatitis is suspected, Byetta should be discontinued. If pancreatitis is confirmed, Byetta should not be restarted unless an alternative etiology is identified.

Early Communication Issued Regarding Atrial Fibrillation With Oral And Intravenous Bisphosphonates

FDA issued an early communication about the ongoing review of new safety data regarding the association of atrial fibrillation with the use of bisphosphonates. Bisphosphonates are a class of drugs used primarily to increase bone mass and reduce the risk for fracture in patients with osteoporosis, slow bone turnover in patients with Paget's

disease of the bone, treat bone metastases, and lower elevated levels of blood calcium in patients with cancer.

FDA reviewed spontaneous postmarketing reports of atrial fibrillation reported in association with oral and intravenous bisphosphonates and did not identify a population of bisphosphonate users at increased risk of atrial fibrillation. In addition, as part of the data review for the recent approval of once-yearly Reclast for the treatment of postmenopausal osteoporosis, FDA evaluated the possible association between atrial fibrillation and the use of Reclast. Most cases of atrial fibrillation occurred more than a month after drug infusion. Also, in a subset of patients monitored by electrocardiogram up to the 11th day following infusion, there was no significant difference in the prevalence of atrial fibrillation between patients who received Reclast and patients who received placebo.

Upon initial review, it is unclear how these data on serious atrial fibrillation should be interpreted. Therefore, FDA does not believe that healthcare providers or patients should change either their prescribing practices or their use of bisphosphonates at this time.

Haloperidol Marketed As Haldol, Haldol Decanoate, And Haldol Lactate Get New Warnings And Revised Prescription Information

Johnson and Johnson and FDA informed healthcare professionals that the WARNINGS section of the prescribing information for haloperidol has been revised to include a new Cardiovascular subsection regarding cases of sudden death, QT prolongation and Torsades de Pointes(TdP) in patients treated with haloperidol, especially when given intravenously, or at doses higher than recommended. Although injectable haloperidol is only approved by the FDA for intramuscular injection, there is considerable evidence that the intravenous administration of haloperidol is a relatively common off-label clinical practice.

There are at least 28 case reports of QT prolongation and TdP, some with fatal outcome in the context of off-label intravenous haloperidol.
Healthcare professionals should consider this new risk information when making individual treatment decisions for their patients.

Fentora (fentanyl buccal tablet) and the occurrence of serious adverse events, including deaths as a result of improper patient selection, improper dosing, and/or improper product substitution

Cephalon issued two Dear Healthcare Professional Letters to inform prescribers and other healthcare providers of important safety information regarding Fentora. Fentora is indicated only for the management of breakthrough pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Serious adverse events, including deaths, have occurred in patients treated with Fentora. These deaths occurred as a result of improper patient selection (e.g., use in opioid non-tolerant patients), improper dosing, and/or improper product substitution. The healthcare professional letters provide key points regarding appropriate patient selection

and proper dosing and administration of Fentora to reduce the risk of respiratory depression.

Next Meeting Information:
Mr. Marascalco reminded the Board of the next meeting scheduled for February 21, 2008.

Mr. Marascalco called for a motion of adjournment at 4:10 p.m. Mr. Strickland made the motion, which was seconded by Dr. Gray. All voted in favor of the motion to adjourn.

Respectfully Submitted:
Health Information Designs

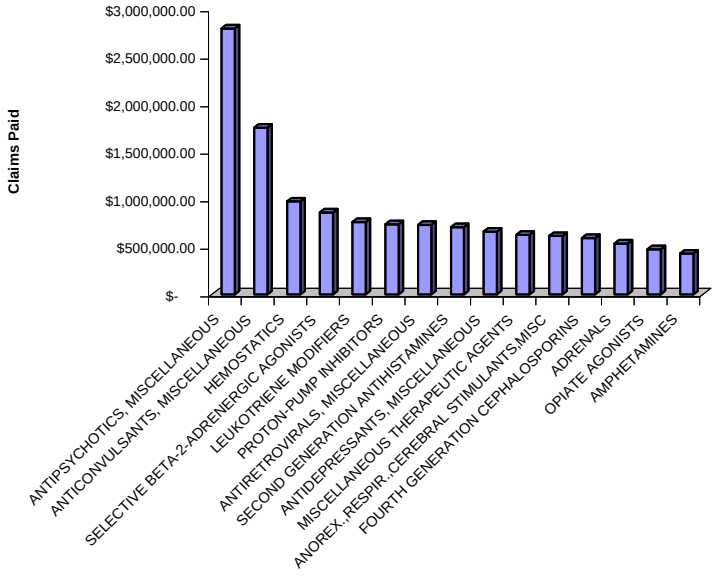
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 09/01/07-09/30/07

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTICS, MISCELLANEOUS	9,421	$ 2,798,383.43	$ 297.04	2.60%
ANTICONVULSANTS, MISCELLANEOUS	10,134	$ 1,754,013.03	$ 173.08	2.80%
HEMOSTATICS	39	$ 977,416.86	$25,061.97	0.01%
SELECTIVE BETA-2-ADRENERGIC AGONISTS	11,794	$ 861,753.68	$ 73.07	3.26%
LEUKOTRIENE MODIFIERS	7,409	$ 760,079.46	$ 102.59	2.05%
PROTON-PUMP INHIBITORS	5,076	$ 737,680.31	$ 145.33	1.40%
ANTIRETROVIRALS, MISCELLANEOUS	1,084	$ 730,533.42	$ 673.92	0.30%
SECOND GENERATION ANTIHISTAMINES	13,204	$ 707,499.46	$ 53.58	3.65%
ANTIDEPRESSANTS, MISCELLANEOUS	12,983	$ 659,200.97	$ 50.77	3.59%
MISCELLANEOUS THERAPEUTIC AGENTS	2,193	$ 626,026.43	$ 285.47	0.61%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	5,374	$ 614,157.89	$ 114.28	1.48%
FOURTH GENERATION CEPHALOSPORINS	11,436	$ 591,644.15	$ 51.74	3.16%
ADRENALS	8,794	$ 534,466.57	$ 60.78	2.43%
OPIATE AGONISTS	24,669	$ 474,692.47	$ 19.24	6.81%
AMPHETAMINES	3,850	$ 428,848.18	$ 111.39	1.06%
TOTAL TOP 15	127,460	$ 13,256,396.31	$ 104.00	35.21%

Total Rx Claims	361,985
From 09/01/07-09/30/07	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



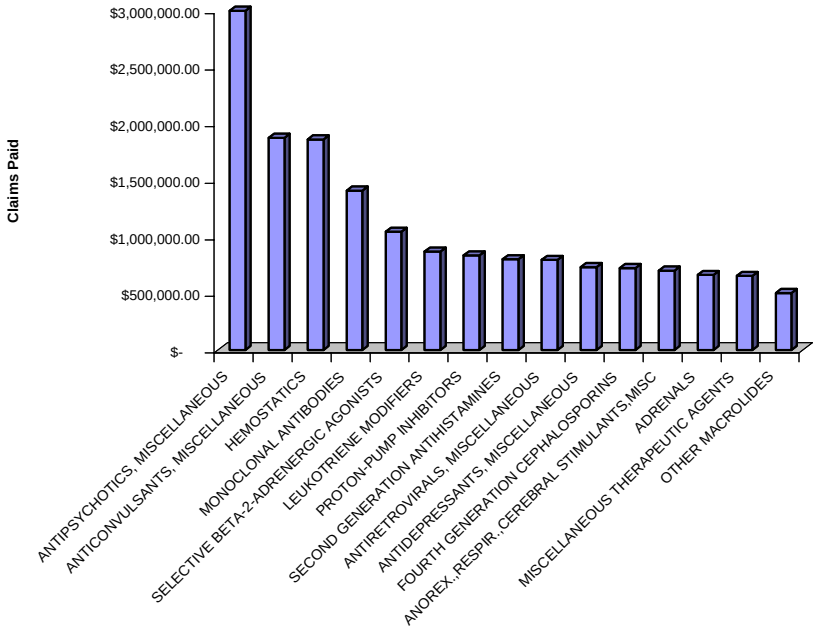
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 10/01/07-10/31/07

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTICS, MISCELLANEOUS	10,227	$ 2,997,412.94	$ 293.09	2.52%
ANTICONVULSANTS, MISCELLANEOUS	10,802	$ 1,874,275.26	$ 173.51	2.66%
HEMOSTATICS	56	$ 1,859,967.02	$33,213.70	0.01%
MONOCLONAL ANTIBODIES	976	$ 1,408,180.53	$ 1,442.81	0.24%
SELECTIVE BETA-2-ADRENERGIC AGONISTS	14,259	$ 1,044,246.78	$ 73.23	3.51%
LEUKOTRIENE MODIFIERS	8,483	$ 869,034.79	$ 102.44	2.09%
PROTON-PUMP INHIBITORS	5,659	$ 835,389.86	$ 147.62	1.39%
SECOND GENERATION ANTIHISTAMINES	15,036	$ 801,292.29	$ 53.29	3.70%
ANTIRETROVIRALS, MISCELLANEOUS	1,163	$ 795,344.68	$ 683.87	0.29%
ANTIDEPRESSANTS, MISCELLANEOUS	14,289	$ 732,675.33	$ 51.28	3.52%
FOURTH GENERATION CEPHALOSPORINS	13,385	$ 722,820.03	$ 54.00	3.29%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	6,162	$ 701,126.60	$ 113.78	1.52%
ADRENALS	10,609	$ 662,664.76	$ 62.46	2.61%
MISCELLANEOUS THERAPEUTIC AGENTS	2,382	$ 654,404.28	$ 274.73	0.59%
OTHER MACROLIDES	13,676	$ 503,132.37	$ 36.79	3.37%
TOTAL TOP 15	127,164	$ 16,461,967.52	$ 129.45	31.30%

Total Rx Claims	406,295
From 10/01/07-10/31/07	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



Health Information Designs, Inc.
1/22/2008

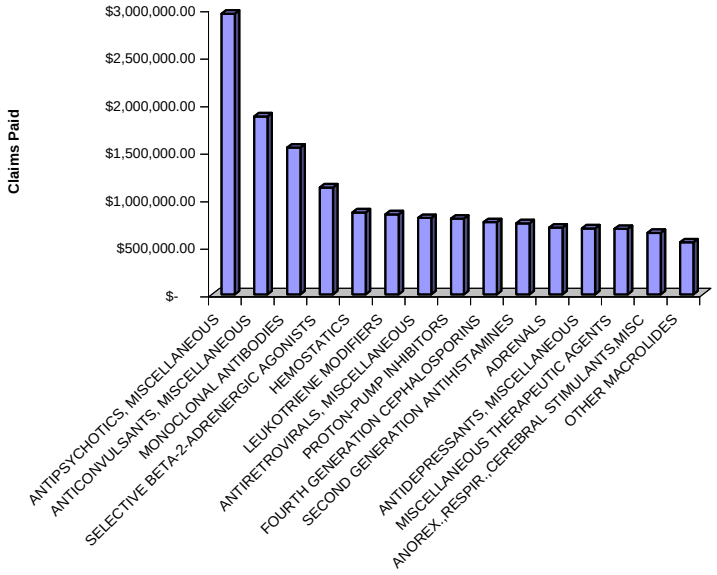
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 11/01/07-11/30/07

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTICS, MISCELLANEOUS	10,068	$ 2,953,154.87	$ 293.32	2.53%
ANTICONVULSANTS, MISCELLANEOUS	10,762	$ 1,873,159.99	$ 174.05	2.71%
MONOCLONAL ANTIBODIES	1,088	$ 1,544,256.21	$ 1,419.35	0.27%
SELECTIVE BETA-2-ADRENERGIC AGONISTS	15,107	$ 1,124,919.40	$ 74.46	3.80%
HEMOSTATICS	34	$ 862,135.58	$25,356.93	0.01%
LEUKOTRIENE MODIFIERS	8,203	$ 841,572.34	$ 102.59	2.06%
ANTIRETROVIRALS, MISCELLANEOUS	1,150	$ 802,548.33	$ 697.87	0.29%
PROTON-PUMP INHIBITORS	5,415	$ 795,846.96	$ 146.97	1.36%
FOURTH GENERATION CEPHALOSPORINS	13,703	$ 758,982.73	$ 55.39	3.44%
SECOND GENERATION ANTIHISTAMINES	14,073	$ 746,554.22	$ 53.05	3.54%
ADRENALS	11,347	$ 702,177.88	$ 61.88	2.85%
ANTIDEPRESSANTS, MISCELLANEOUS	13,621	$ 693,912.97	$ 50.94	3.42%
MISCELLANEOUS THERAPEUTIC AGENTS	2,246	$ 688,545.25	$ 306.57	0.56%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	5,614	$ 646,790.69	$ 115.21	1.41%
OTHER MACROLIDES	14,967	$ 546,698.25	$ 36.53	3.76%
TOTAL TOP 15	127,398	$ 15,581,255.67	$ 122.30	32.02%

Total Rx Claims From 11/01/07-11/30/07	397,855

Top 15 Therapeutic Classes
Based on Total Cost of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

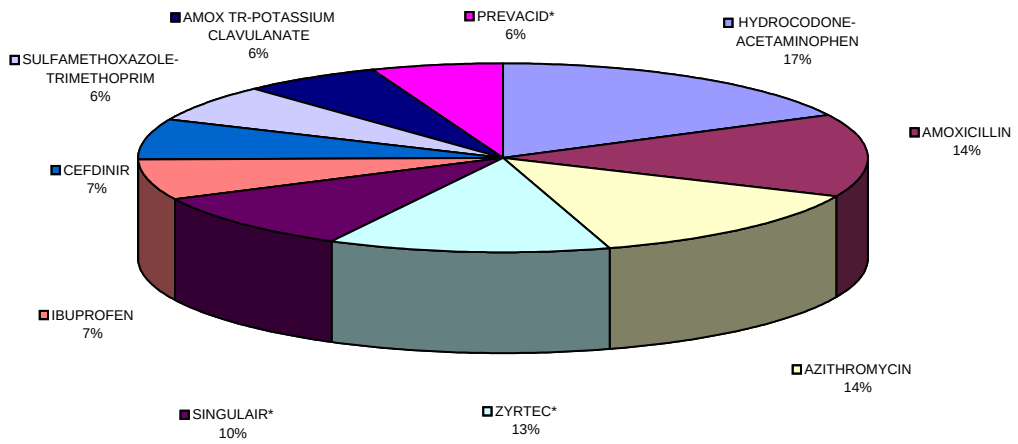
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 09/01/07-09/30/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	13,227	$ 136,480.99	1
AMOXICILLIN	EXTENDED-SPECTRUM PENICILLINS	10,476	$ 98,818.64	3
AZITHROMYCIN	OTHER MACROLIDES	10,292	$ 360,736.51	9
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	9,443	$ 546,484.65	12
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,403	$ 759,192.84	7
IBUPROFEN	OTHER NONSTEROIDAL ANTI-INFLAM. AGENTS	5,291	$ 42,571.16	13
CEFDINIR	FOURTH GENERATION CEPHALOSPORINS	5,187	$ 379,890.76	--------
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	4,740	$ 55,837.42	40
AMOX TR-POTASSIUM CLAVULANATE	EXTENDED-SPECTRUM PENICILLINS	4,539	$ 242,633.97	22
PREVACID*	PROTON-PUMP INHIBITORS	4,450	$ 653,860.38	8
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,271	$ 35,506.19	7
ED A-HIST	PROPYLAMINE DERIVATIVES	3,924	$ 34,828.85	-------
CEPHALEXIN	FOURTH GENERATION CEPHALOSPORINS	3,592	$ 58,775.42	14
ALBUTEROL SULFATE	SELECTIVE BETA-2-ADRENERGIC AGONISTS	3,454	$ 87,420.53	61
ACETAMINOPHEN-CODEINE	OPIATE AGONISTS	3,222	$ 25,751.36	31
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,140	$ 60,365.94	23
ADDERALL XR*	AMPHETAMINES	3,028	$ 381,824.90	42
RISPERDAL*	ANTIPSYCHOTICS, MISCELLANEOUS	3,015	$ 821,285.60	48
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	2,984	$ 35,793.18	53
ALBUTEROL	SELECTIVE BETA-2-ADRENERGIC AGONISTS	2,764	$ 69,007.59	106
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,707	$ 71,546.49	19
FERROUS SULFATE	IRON PREPARATIONS	2,641	$ 9,588.52	106
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	2,575	$ 97,658.87	119
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,545	$ 81,308.15	42
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,433	$ 306,342.00	46
TOTAL TOP 25		121,343	$ 5,453,510.91	

Total Rx Claims From 09/01/07-09/30/07	361,985

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

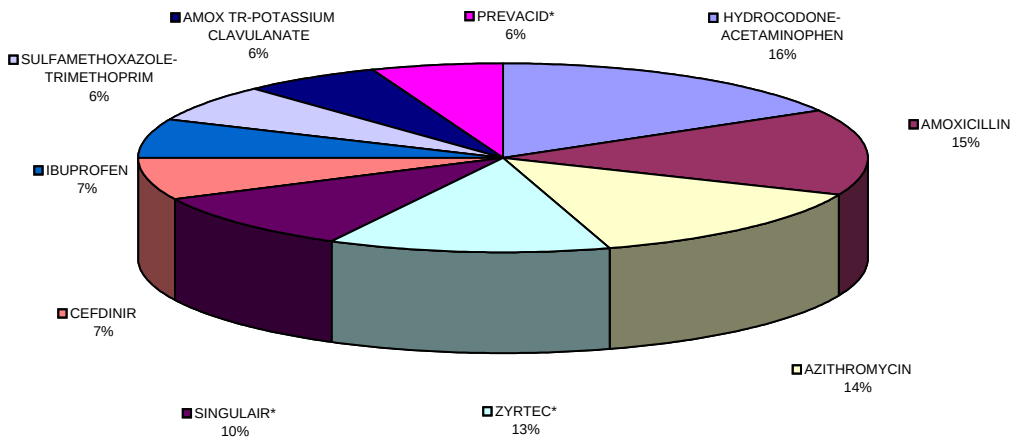
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 10/01/07-10/31/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	14,284	$ 147,045.21	1
AMOXICILLIN	EXTENDED-SPECTRUM PENICILLINS	12,669	$ 121,547.43	3
AZITHROMYCIN	OTHER MACROLIDES	11,877	$ 422,158.04	9
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	10,782	$ 618,060.63	12
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,478	$ 868,235.64	7
CEFDINIR	FOURTH GENERATION CEPHALOSPORINS	6,247	$ 462,207.41	------
IBUPROFEN	OTHER NONSTEROIDAL ANTI-INFLAM. AGENTS	5,674	$ 46,262.10	13
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	5,452	$ 64,749.34	40
AMOX TR-POTASSIUM CLAVULANATE	EXTENDED-SPECTRUM PENICILLINS	5,340	$ 285,759.79	22
PREVACID*	PROTON-PUMP INHIBITORS	4,961	$ 738,948.81	8
ED A-HIST	PROPYLAMINE DERIVATIVES	4,960	$ 43,626.14	------
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,750	$ 39,862.97	7
ALBUTEROL SULFATE	SELECTIVE BETA-2-ADRENERGIC AGONISTS	4,429	$ 109,319.98	61
CEPHALEXIN	FOURTH GENERATION CEPHALOSPORINS	3,924	$ 63,689.45	14
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	3,750	$ 44,011.70	53
ACETAMINOPHEN-CODEINE	OPIATE AGONISTS	3,615	$ 28,744.34	31
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,411	$ 65,252.44	23
ADDERALL XR*	AMPHETAMINES	3,296	$ 437,284.52	42
RISPERDAL*	ANTIPSYCHOTICS, MISCELLANEOUS	3,249	$ 873,716.84	48
ALBUTEROL	SELECTIVE BETA-2-ADRENERGIC AGONISTS	3,068	$ 78,135.04	11
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,929	$ 78,886.61	19
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,878	$ 93,044.48	42
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	2,866	$ 108,149.10	119
FERROUS SULFATE	IRON PREPARATIONS	2,862	$ 10,258.40	106
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,778	$ 349,624.20	46
TOTAL TOP 25		138,529	$ 6,198,580.61	

Total Rx Claims From 10/01/07-10/31/07	406,295

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

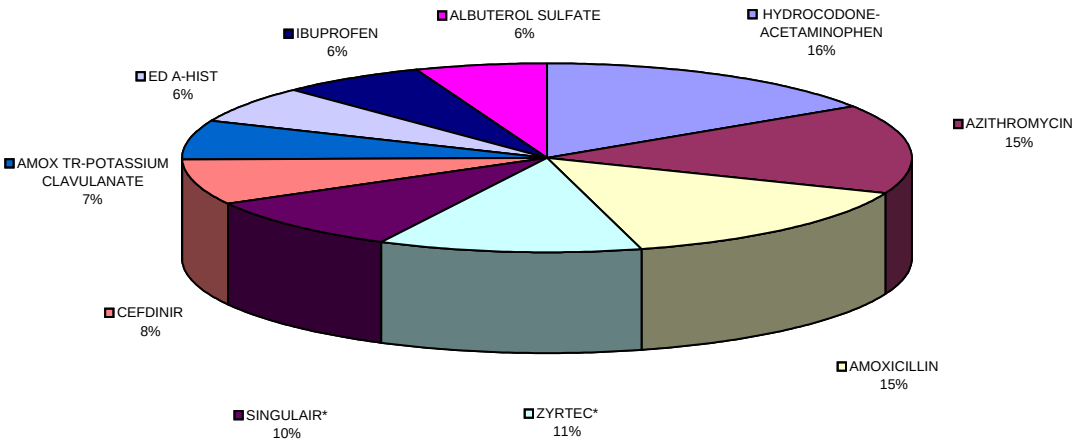
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 11/01/07-11/30/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	13,724	$ 144,879.62	1
AZITHROMYCIN	OTHER MACROLIDES	12,995	$ 460,730.87	9
AMOXICILLIN	EXTENDED-SPECTRUM PENICILLINS	12,739	$ 122,540.42	3
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	9,881	$ 569,052.93	12
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,198	$ 840,955.59	7
CEFDINIR	FOURTH GENERATION CEPHALOSPORINS	6,680	$ 491,715.59	------
AMOX TR-POTASSIUM CLAVULANATE	EXTENDED-SPECTRUM PENICILLINS	5,744	$ 304,998.58	22
ED A-HIST	PROPYLAMINE DERIVATIVES	5,539	$ 48,368.38	------
IBUPROFEN	OTHER NONSTEROIDAL ANTI-INFLAM. AGENTS	5,430	$ 44,435.12	13
ALBUTEROL SULFATE	SELECTIVE BETA-2-ADRENERGIC AGONISTS	5,071	$ 122,399.93	61
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	4,895	$ 57,621.86	40
PREVACID*	PROTON-PUMP INHIBITORS	4,807	$ 714,568.76	8
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,724	$ 39,889.68	7
CEPHALEXIN	FOURTH GENERATION CEPHALOSPORINS	3,579	$ 57,051.19	14
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,397	$ 64,874.11	23
ACETAMINOPHEN-CODEINE	OPIATE AGONISTS	3,375	$ 26,883.22	31
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	3,322	$ 40,367.02	53
RISPERDAL*	ANTIPSYCHOTICS, MISCELLANEOUS	3,273	$ 878,614.69	48
ADDERALL XR*	AMPHETAMINES	3,041	$ 412,454.67	42
ALBUTEROL	SELECTIVE BETA-2-ADRENERGIC AGONISTS	2,862	$ 73,400.56	11
PREDNISOLONE	ADRENALS	2,812	$ 35,152.20	132
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	2,773	$ 77,432.98	19
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,707	$ 85,518.57	42
FERROUS SULFATE	IRON PREPARATIONS	2,707	$ 9,603.42	106
XOPENEX*	SELECTIVE BETA-2-ADRENERGIC AGONISTS	2,689	$ 461,766.23	131
TOTAL TOP 25		136,964	$ 6,185,276.19	

Total Rx Claims From 11/01/07-11/30/07	397,855

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

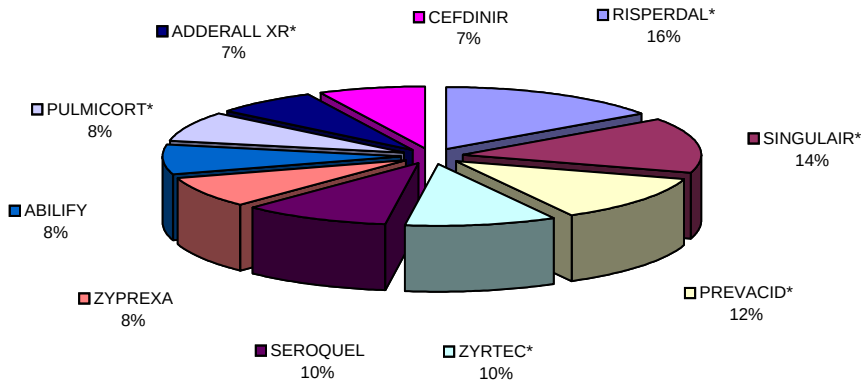
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 09/01/07-09/30/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
RISPERDAL*	ANTIPSYCHOTICS, MISCELLANEOUS	3,015	$ 821,285.60	18
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,403	$ 759,192.84	5
PREVACID*	PROTON-PUMP INHIBITORS	4,450	$ 653,860.38	3
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	9,443	$ 546,484.65	29
SEROQUEL	ANTIPSYCHOTICS, MISCELLANEOUS	1,681	$ 531,816.56	11
ZYPREXA	ANTIPSYCHOTICS, MISCELLANEOUS	896	$ 436,186.74	19
ABILIFY	ANTIPSYCHOTICS, MISCELLANEOUS	950	$ 417,321.93	24
PULMICORT*	ADRENALS	1,721	$ 405,830.67	73
ADDERALL XR*	AMPHETAMINES	3,028	$ 381,824.90	33
CEFDINIR	FOURTH GENERATION CEPHALOSPORINS	5,187	$ 379,890.76	-------
AZITHROMYCIN	OTHER MACROLIDES	10,292	$ 360,736.51	3
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,159	$ 347,967.03	20
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,433	$ 306,342.00	41
XOPENEX*	SELECTIVE BETA-2-ADRENERGIC AGONISTS	1,713	$ 287,344.02	107
ADVAIR DISKUS*	SELECTIVE BETA-2-ADRENERGIC AGONISTS	1,553	$ 275,687.27	4
GEODON*	ANTIPSYCHOTICS, MISCELLANEOUS	795	$ 256,840.97	72
ADVATE	HEMOSTATICS	7	$ 242,639.22	-------
AMOX TR-POTASSIUM CL	EXTENDED-SPECTRUM PENICILLINS	4,539	$ 242,633.97	6
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	744	$ 237,079.75	26
EXJADE	HEAVY METAL ANTAGONISTS	53	$ 222,907.58	-------
TRILEPTAL*	ANTICONVULSANTS, MISCELLANEOUS	1,119	$ 214,636.64	74
FEIBA VH IMMUNO	HEMOSTATICS	4	$ 213,379.99	-------
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	1,787	$ 201,860.49	5
STRATTERA*	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,298	$ 195,455.43	63
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	782	$ 186,233.51	81
TOTAL TOP 25		66,052	$ 9,125,439.41	

Total Rx Claims From 09/01/07-09/30/07	361,985

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

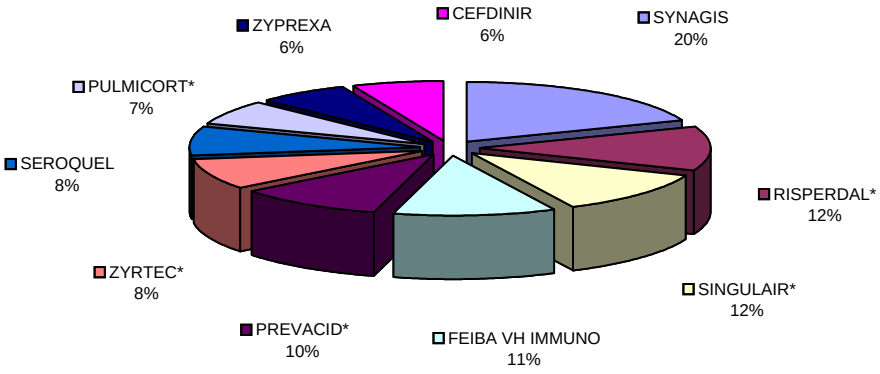
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 10/01/07-10/31/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
SYNAGIS	MONOCLONAL ANTIBODIES	976	$ 1,408,180.53	-------
RISPERDAL*	ANTIPSYCHOTICS, MISCELLANEOUS	3,249	$ 873,716.84	18
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,478	$ 868,235.64	5
FEIBA VH IMMUNO	HEMOSTATICS	11	$ 844,940.59	-------
PREVACID*	PROTON-PUMP INHIBITORS	4,961	$ 738,948.81	3
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	10,782	$ 618,060.63	29
SEROQUEL	ANTIPSYCHOTICS, MISCELLANEOUS	1,795	$ 565,031.46	11
PULMICORT*	ADRENALS	2,150	$ 509,538.82	73
ZYPREXA	ANTIPSYCHOTICS, MISCELLANEOUS	949	$ 468,062.10	19
CEFDINIR	FOURTH GENERATION CEPHALOSPORINS	6,247	$ 462,207.41	-------
ADDERALL XR*	AMPHETAMINES	3,296	$ 437,284.52	33
ABILIFY	ANTIPSYCHOTICS, MISCELLANEOUS	976	$ 431,763.94	24
AZITHROMYCIN	OTHER MACROLIDES	11,877	$ 422,158.04	3
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,248	$ 370,907.64	20
XOPENEX*	SELECTIVE BETA-2-ADRENERGIC AGONISTS	2,214	$ 370,247.42	107
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,778	$ 349,624.20	41
ADVAIR DISKUS*	SELECTIVE BETA-2-ADRENERGIC AGONISTS	1,673	$ 309,935.06	4
AMOX TR-POTASSIUM CL	EXTENDED-SPECTRUM PENICILLINS	5,340	$ 285,759.79	6
GEODON*	ANTIPSYCHOTICS, MISCELLANEOUS	845	$ 270,997.26	72
ADVATE	HEMOSTATICS	11	$ 266,051.62	-------
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	808	$ 246,760.09	26
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	1,851	$ 214,201.70	5
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	843	$ 207,534.79	81
STRATTERA*	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,396	$ 207,347.52	63
EFFEXOR XR*	ANTIDEPRESSANTS, MISCELLANEOUS	1,304	$ 198,001.45	6
TOTAL TOP 25		76,058	$ 11,945,497.87	

Total Rx Claims From 10/01/07-10/31/07	406,295

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

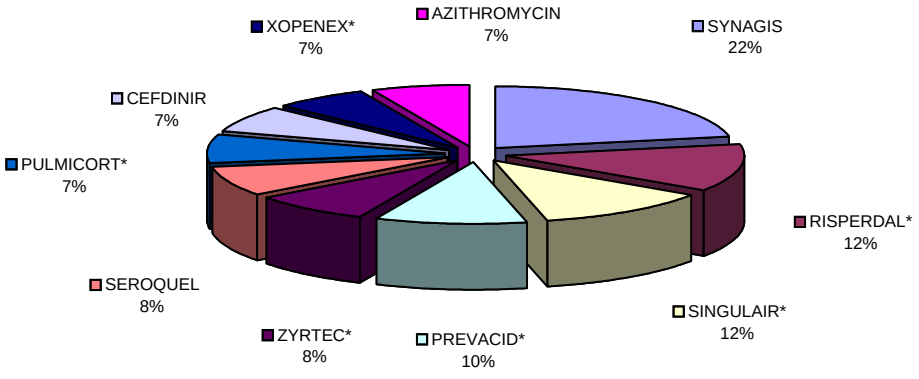
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 11/01/07-11/30/07

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
SYNAGIS	MONOCLONAL ANTIBODIES	1,088	$ 1,544,256.21	-------
RISPERDAL*	ANTIPSYCHOTICS, MISCELLANEOUS	3,273	$ 878,614.69	18
SINGULAIR*	LEUKOTRIENE MODIFIERS	8,198	$ 840,955.59	5
PREVACID*	PROTON-PUMP INHIBITORS	4,807	$ 714,568.76	3
ZYRTEC*	SECOND GENERATION ANTIHISTAMINES	9,881	$ 569,052.93	29
SEROQUEL	ANTIPSYCHOTICS, MISCELLANEOUS	1,742	$ 552,658.56	11
PULMICORT*	ADRENALS	2,167	$ 523,188.82	73
CEFDINIR	FOURTH GENERATION CEPHALOSPORINS	6,680	$ 491,715.59	-------
XOPENEX*	SELECTIVE BETA-2-ADRENERGIC AGONISTS	2,689	$ 461,766.23	107
AZITHROMYCIN	OTHER MACROLIDES	12,995	$ 460,730.87	3
ZYPREXA	ANTIPSYCHOTICS, MISCELLANEOUS	901	$ 438,708.09	19
ABILIFY	ANTIPSYCHOTICS, MISCELLANEOUS	964	$ 420,059.62	24
ADDERALL XR*	AMPHETAMINES	3,041	$ 412,454.67	33
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,288	$ 374,237.82	20
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,469	$ 314,450.80	41
AMOX TR-POTASSIUM CL	EXTENDED-SPECTRUM PENICILLINS	5,744	$ 304,998.58	6
ADVAIR DISKUS*	SELECTIVE BETA-2-ADRENERGIC AGONISTS	1,621	$ 299,759.06	4
GEODON*	ANTIPSYCHOTICS, MISCELLANEOUS	850	$ 272,324.49	72
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	818	$ 253,091.41	26
FEIBA VH IMMUNO	HEMOSTATICS	2	$ 225,894.46	-------
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	832	$ 214,892.55	81
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	1,841	$ 208,763.61	5
STRATTERA*	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,312	$ 197,089.21	63
EFFEXOR XR*	ANTIDEPRESSANTS, MISCELLANEOUS	1,221	$ 190,280.79	6
DEPAKOTE*	ANTICONVULSANTS, MISCELLANEOUS	974	$ 186,729.70	69
TOTAL TOP 25		77,398	$ 11,351,243.11	

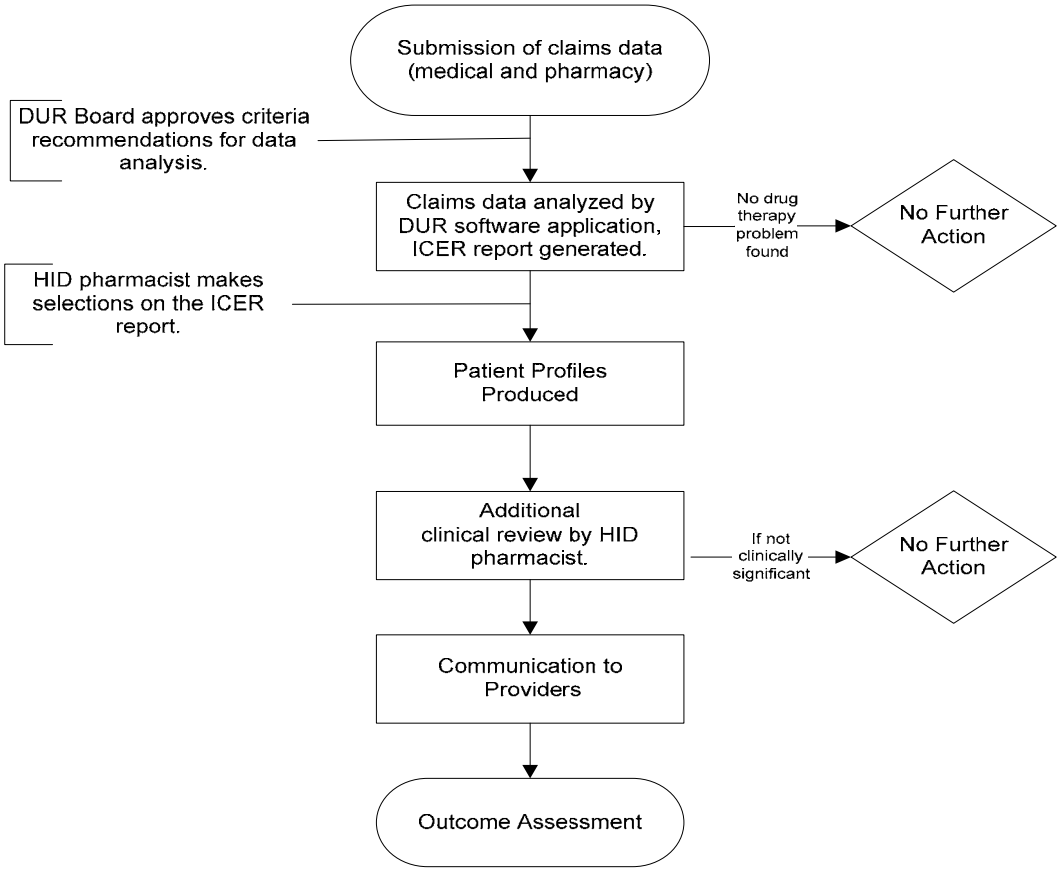
Total Rx Claims From 11/01/07-11/30/07	397,855

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



Overview of Retrospective Drug Utilization Review (RDUR) Intervention Process



Steps

- Paid Medicaid claims are submitted to HID by DOM's claims administrator.
- The therapeutic RDUR criteria, which are reviewed and approved by the DUR Board, are applied to each recipient record.
- An Initial Criteria Exception Report (ICER) is generated to aid in the selection of high risk profiles. An HID clinical pharmacist selects profiles for review.
- Selected patient profiles are generated.
- Each patient profile is reviewed by a clinical pharmacist to verify clinical significance. Profiles are coded for either action or no action.
- Each coded profile is again reviewed by a different pharmacist for quality control.
- Intervention letters and profiles are sent to appropriate providers. Providers are asked to provide feedback as to the action resulting from the letter.
- Activity and response are reported to DOM monthly and quarterly.

Office of the Governor
Division of Medicaid

Administered by Health Information Designs, Inc.
PO Box 320506
Flowood, MS 39232
(800) 355-0486 Fax (800) 459-2135

Drug Utilization Review Program

February 21, 2008

Doe, John MD
100 Capital
Jackson, MS 39211

DEAR PRESCRIBER DOE:

Health Information Designs, Inc. (HID) is the pharmacy benefits management/drug utilization review organization contracted with the Mississippi Division of Medicaid (DOM) to review pharmacy services provided to Medicaid beneficiaries. Under this contract, we seek to ensure that Medicaid beneficiaries receive appropriate and cost effective drug therapy. One way to achieve this goal is to identify potential drug therapy problems that may place patients at risk, particularly if multiple providers are identified. **This letter is educational in nature and allows you to incorporate the information provided into your continuing assessment of the patient's drug therapy.**

During a recent review of the enclosed drug history profile, *it was noted your patient,* **JANE DOE**, *is receiving drug(s):* **LOTREL**. Angiotensin-converting enzyme inhibitors (ACEIs) are not recommended during pregnancy due to the possible risk of fetal abnormalities in humans. ACEIs should be used only if the benefits outweigh the risks of harm to the fetus. All ACEIs are FDA pregnancy category C during the first trimester and pregnancy category D during the second and third trimesters. In presenting this information to you, we recognize that the management of each patient's drug therapy depends upon an assessment of the patient's entire clinical situation about which we are not fully aware.

The success of the DUR program is enhanced by effective two-way exchange of information. Therefore, at your convenience, we would appreciate learning of your assessment of this information and of any action taken in response to this notice. Although your participation in this program is voluntary, we find your feedback helpful in adjusting our program to address clinically important problems. Please complete the response form on the reverse side of this letter and return it in the enclosed envelope or fax it to the number above.

At the bottom of this letter are the specific prescriptions attributed to you by the dispensing pharmacy. In addition, if multiple prescribers are involved in the therapy identified above, each will receive this information. Thank you for your professional consideration.

RX #(s): 1234567

Sincerely,

W. Murray Yarbrough M.D.

W. Murray Yarbrough, M.D.
Medical Director
Health Information Designs, Inc.

Case#: 11111
Enclosures

Office of the Governor
Division of Medicaid

Administered by Health Information Designs, Inc.
PO Box 320506
Flowood, MS 39232
(800) 355-0486 Fax (800) 459-2135

Drug Utilization Review Program

PRESCRIBER RESPONSE

All information used to generate the enclosed letter, including Prescriber identification, was obtained from Pharmacy Claims Data. If there appears to be an error in the information provided, please note the discrepancy. Thank you for your cooperation.

1. This patient **is** under my care:

_____ I have reviewed the information and will continue without change.
_____ however, I did not prescribe the following medication(s) _____.
_____ and has an appointment to discuss drug therapy.
_____ however, has not seen me recently.
_____ however, I was not aware of other prescribers.
_____ I have reviewed the information and modified drug therapy.
_____ I have not modified drug therapy because benefits outweigh the risks.
_____ I have tried to modify therapy; however the patient refuses to change.
_____ I have tried to modify therapy, however symptoms reoccurred.

2. This patient **is not** under my care:

_____ however, I did prescribe medication while covering for other MD or in the ER.
_____ but has previously been a patient of mine.
_____ because the patient recently expired.
_____ and has never been under my care.

3. I have reviewed the enclosed information and found it:
_____ very useful_____ useful_____ neutral_____ somewhat useful_____ not useful.

4. Please check here if you wish to receive reference information on the identified problem___. (Please provide a fax number if available_____-_____-_____.)

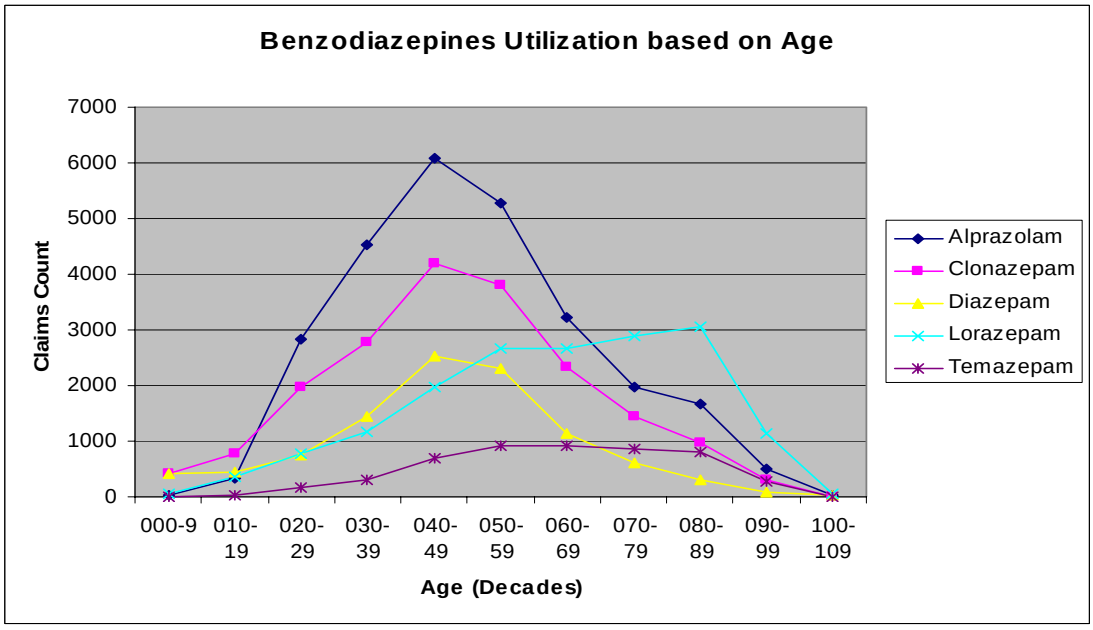
Comments: _____
_____
_____
_____

DOE, JOHN MD Case# 11111
Letter Type 99
Angiotensin-converting enzyme inhibitors (ACEIs) are not recommended during pregnancy due to the possible risk of fetal abnormalities in humans. ACEIs should be used only if the benefits outweigh the risks of harm to the fetus. All ACEIs are FDA pregnancy category C during the first trimester and pregnancy category D during the second and third trimesters.
124

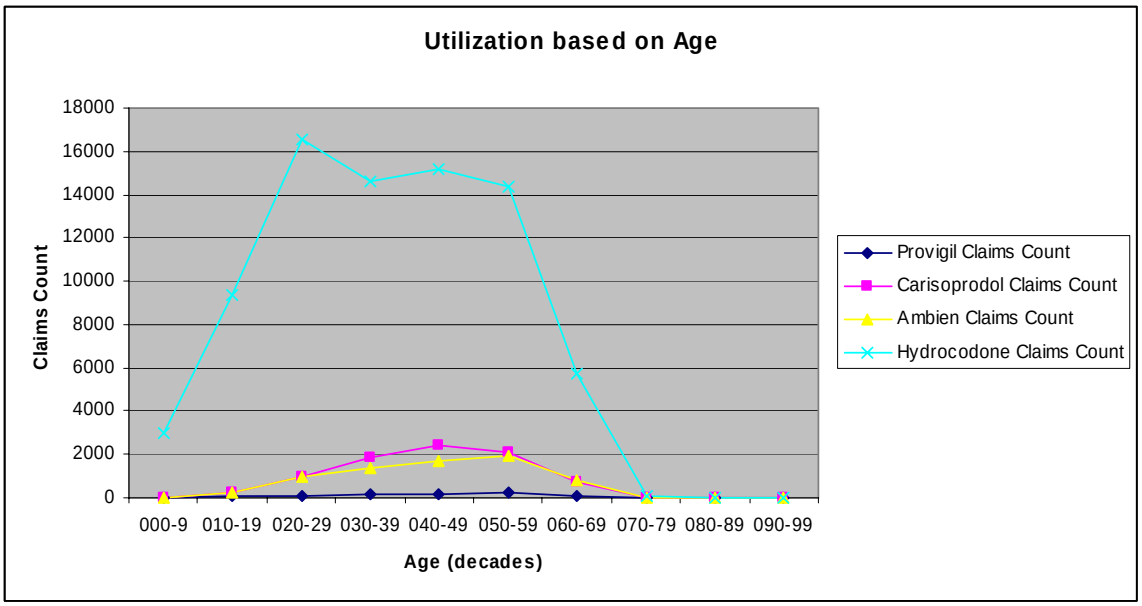
Common Drugs of Abuse and Their Utilization within the MS Medicaid Population

At the November DUR Board Meeting, HID presented some data regarding hydrocodone, alprazolam, and lorazepam utilization in response to specific requests from the Pharmacy Bureau of MS Medicaid. This presentation of data sparked some very interesting conversations, thoughts, and questions during the meeting. It also left the Board with many questions in regards to the utilization of not only these medications, but others that are commonly abused. As a result, HID has conducted a more thorough and in-depth analysis of this data to provide insight on what the current trends are regarding these medications and to help answer those questions raised at the last DUR Board Meeting.

1) How does utilization of these drugs appear based on age?



As the graph above shows, the largest age group that uses the benzodiazepines is the 40-49 age group, with the exception of lorazepam and temazepam. Lorazepam use is strongest among the 80-89 age group, which is not surprising due to its extensive use in the elderly population. Temazepam's utilization peaks with the 50-59 age group and remains at that same level through the 80-89 age group. Once again, this is not surprising due to the higher incidence of insomnia in the elderly population.



Hydrocodone
According to the chart above, hydrocodone utilization is greatest among the 20-29 year olds, but there is considerable use in the 30-59 age category as well, with use falling sharply after the 50-59 age group.

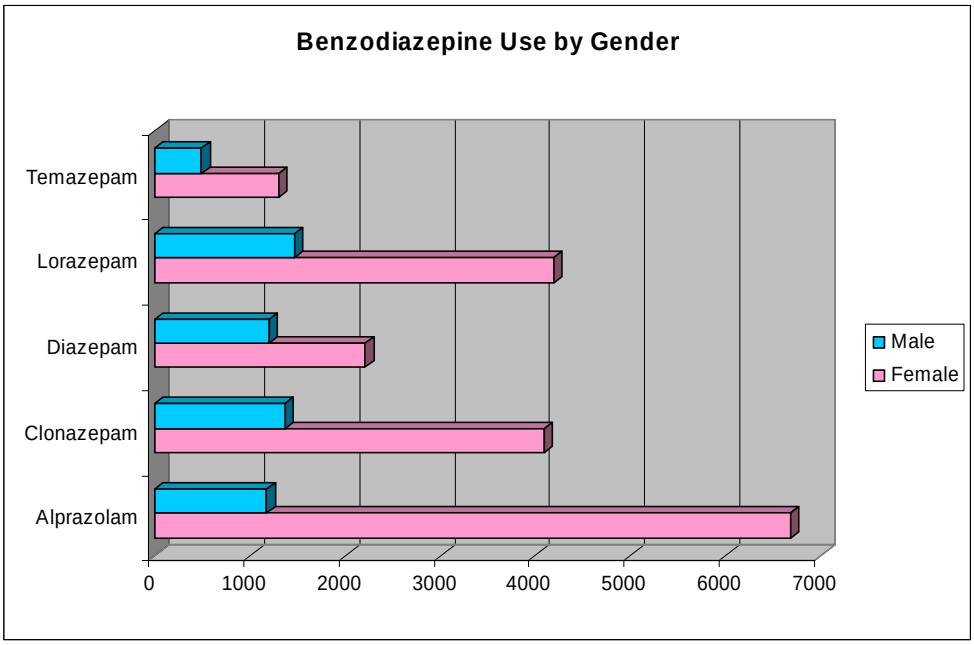
Provigil®
Utilization of Provigil® is highest among the 50-59 age category, reflecting the increased incidence of obstructive sleep apnea in individuals over the age of 40. There is also considerable use in the 30-39 age group, which may reflect both narcolepsy and obstructive sleep apnea diagnoses, the FDA-approved indications for Provigil®.

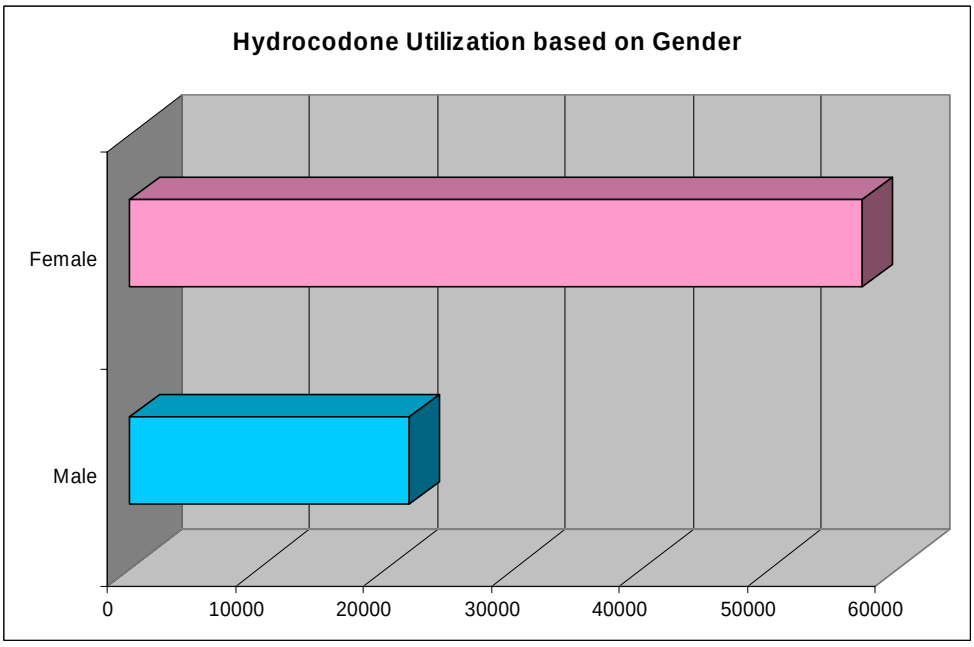
Carisoprodol
Carisoprodol utilization peaks among the 40-49 year olds.

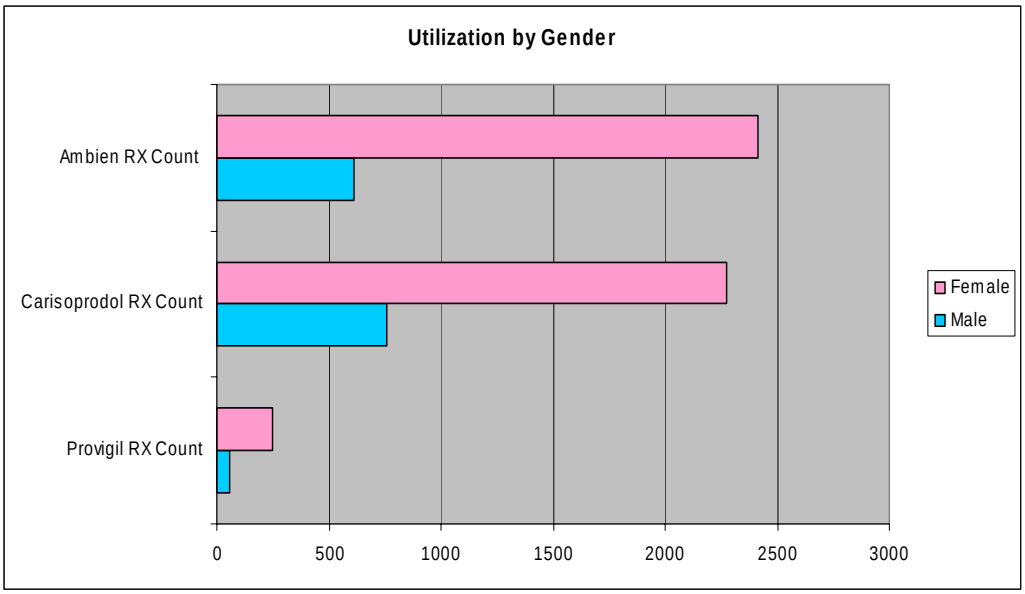
Zolpidem
Utilization of zolpidem (Ambien®) climbs steadily until it peaks with the most use in the 50-59 age group. This is consistent with the higher incidence of insomnia that is seen as age increases.

Summary
With the exception of hydrocodone and lorazepam, the highest utilization of these medications occurs among the 40-59 age group.

2) How does utilization of these drugs appear based on gender?



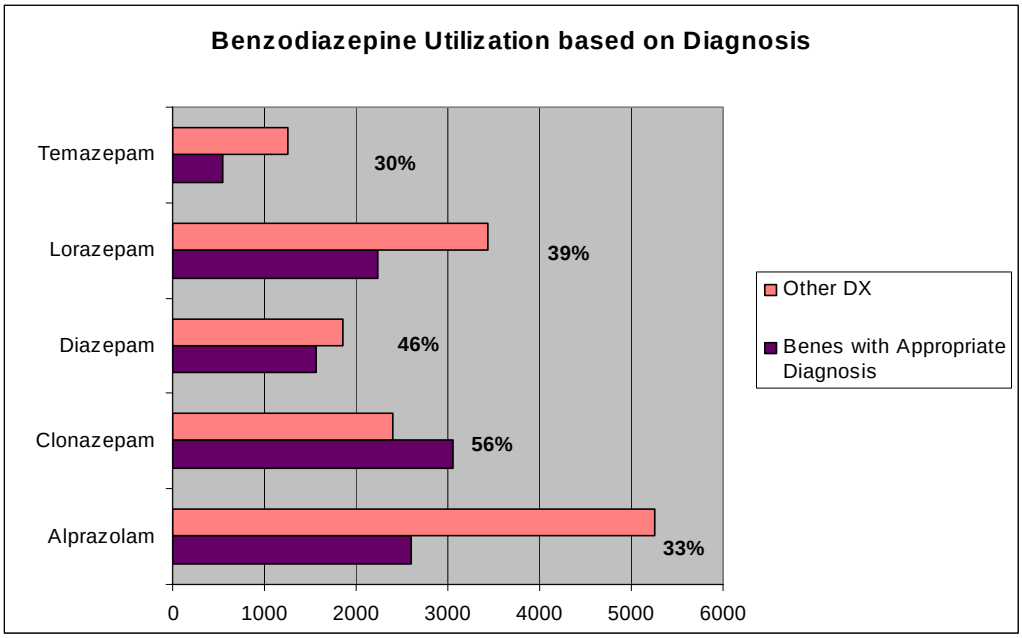




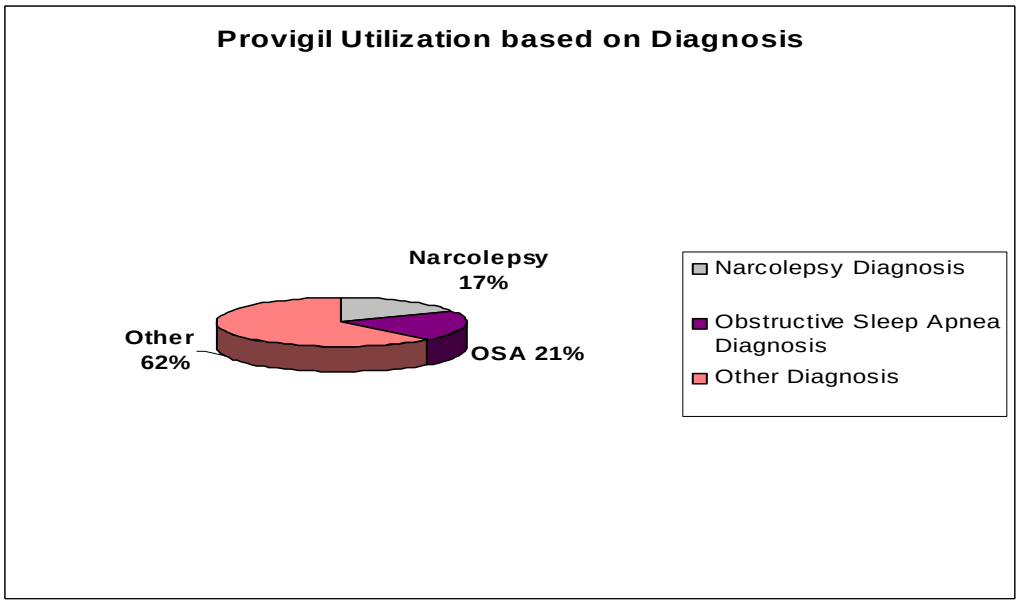
Summary

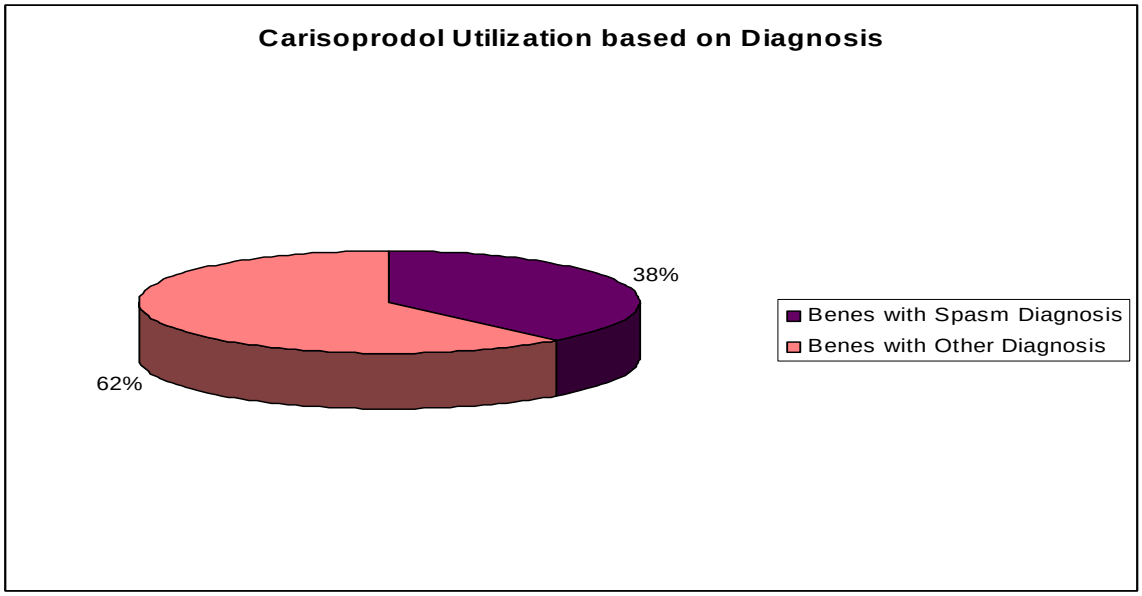
Based on the illustrations below, in all cases, females are clearly the most common recipients of these medications.

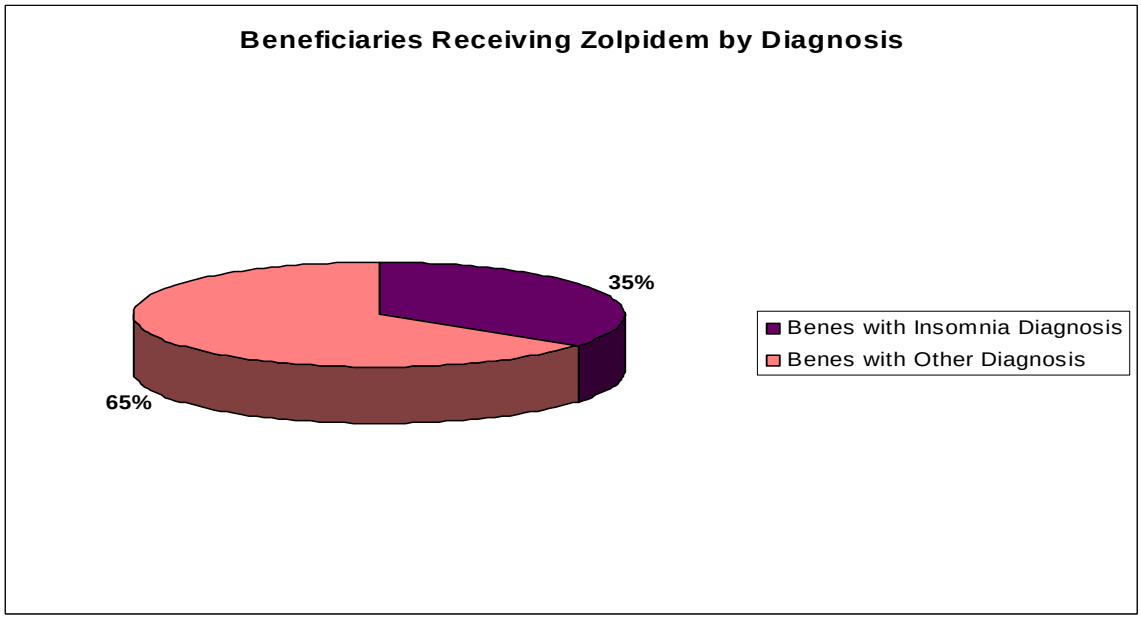
3) Do the beneficiaries that receive these drugs have the appropriate diagnosis that corresponds with the indications for that medication?



At least one-third of all MS Medicaid beneficiaries who receive a benzodiazepine have a diagnosis that is in line with the approved indications for that drug. For clonazepam and diazepam the percentage is even greater, with 56% and 46% of beneficiaries, respectively, having an appropriate diagnosis that warrants use of these medications.



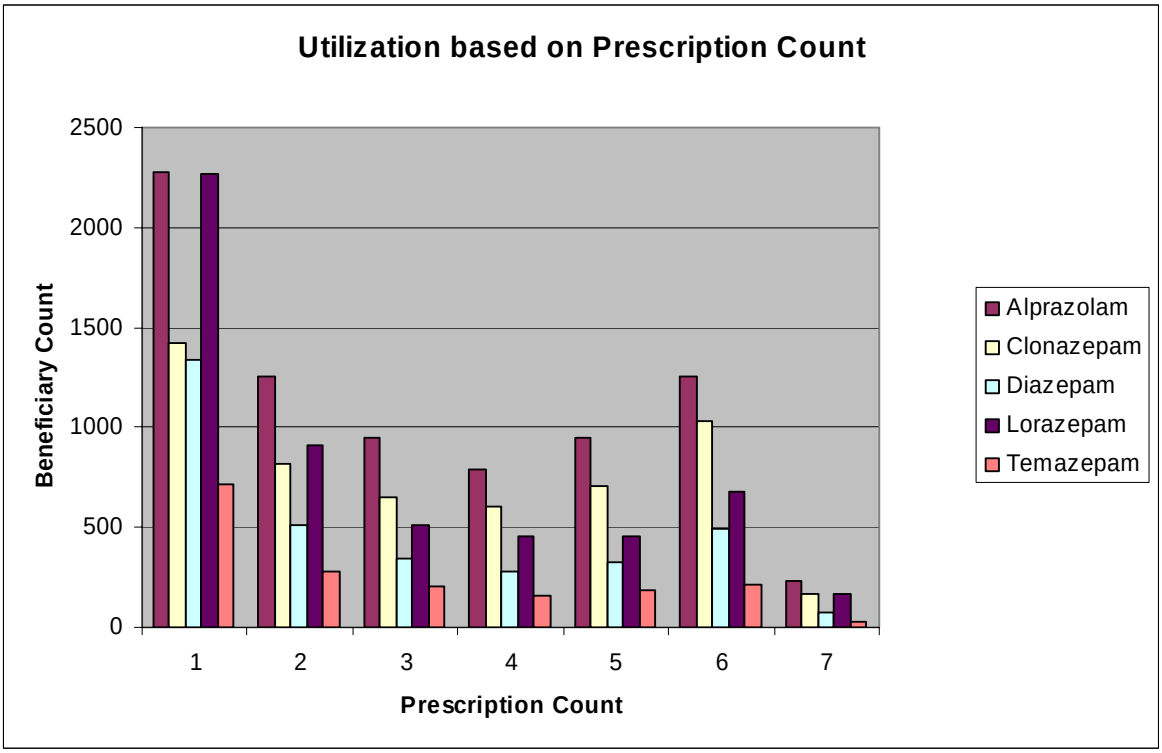




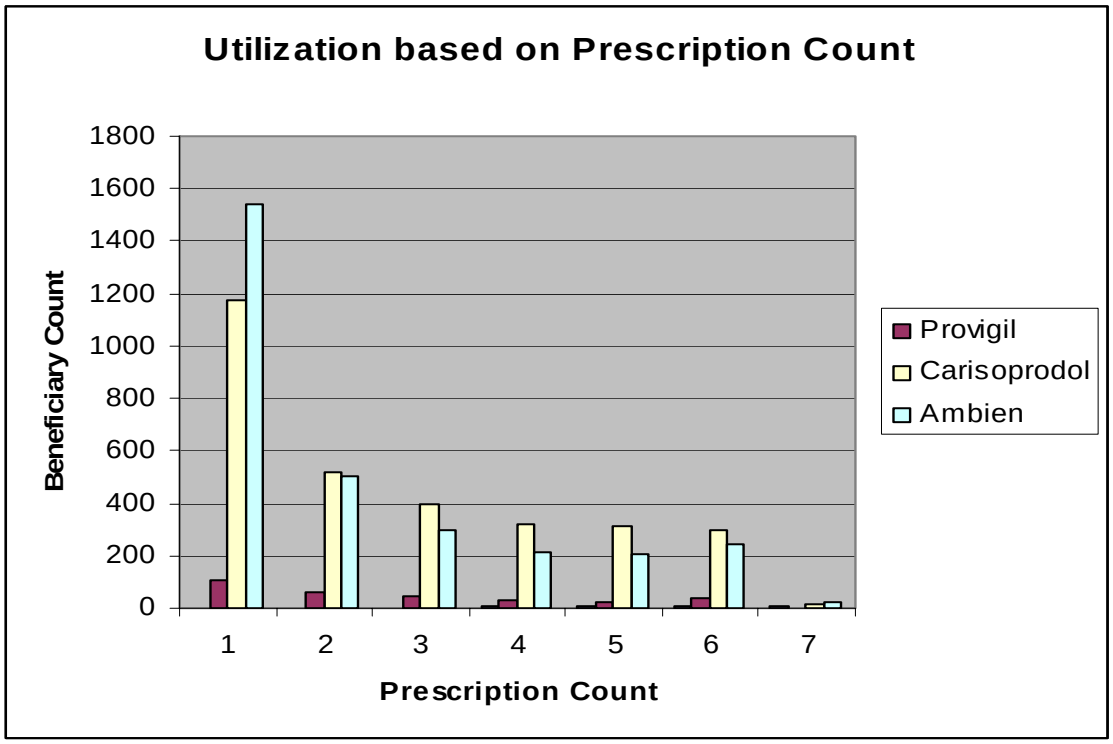
Provigil®, Carisoprodol and Zolpidem
For all 3 of these medications, approximately one-third of MS Medicaid beneficiaries who receiving them had a diagnosis that correlated with their respective FDA-approved indications.

4) What is the prescription count per beneficiary related to these drugs?

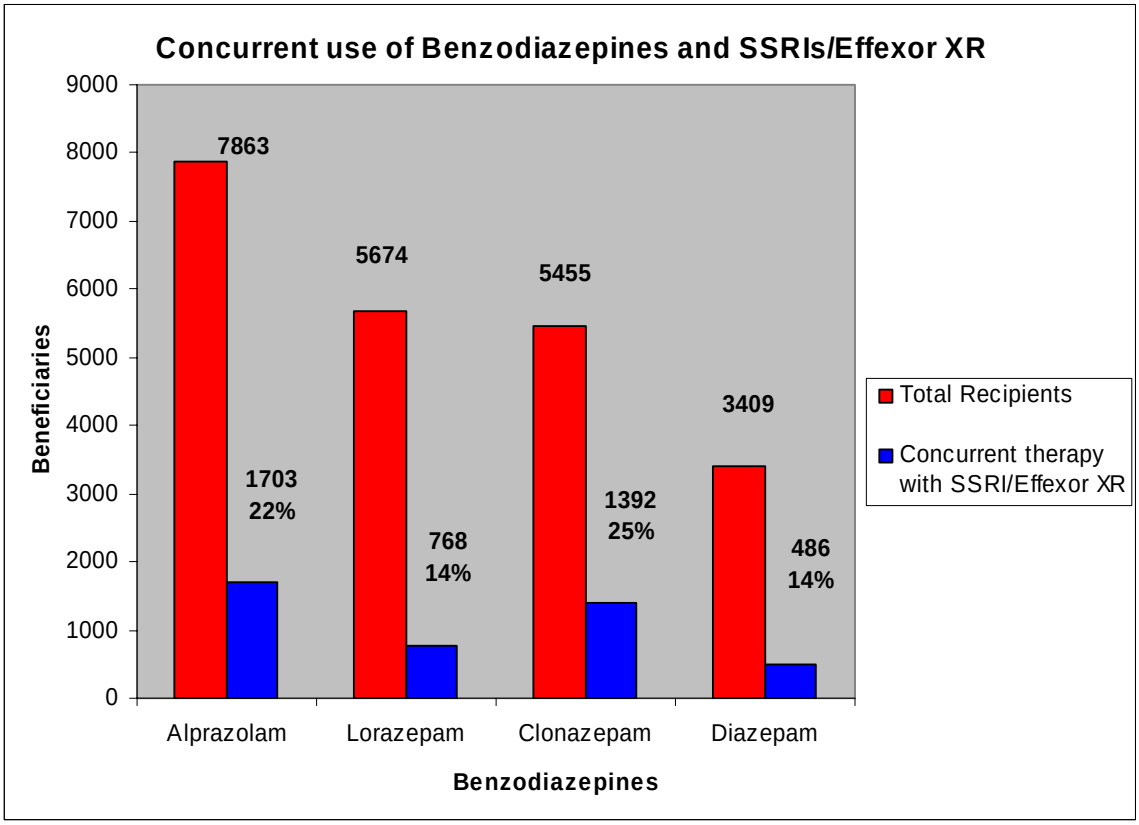
Prescription Count	Alprazolam	Clonazepam	Diazepam	Lorazepam	Temazepam
1	2280	1418	1342	2270	720
2	1258	818	513	908	278
3	944	655	342	511	205
4	786	600	282	454	155
5	944	709	323	454	189
6	1258	1036	494	681	214
7	236	164	71	170	24
8	31	27	14	40	6
9	23	11	15	28	1
≥10	30	45	13	79	2



Prescription Count	Provigil	Carisoprodol	Ambien
1	106	1175	1537
2	63	520	501
3	49	393	298
4	28	320	217
5	25	310	209
6	35	295	245
7	1	19	22
8	1	2	3
9	1	3	1
≥10	0	3	2

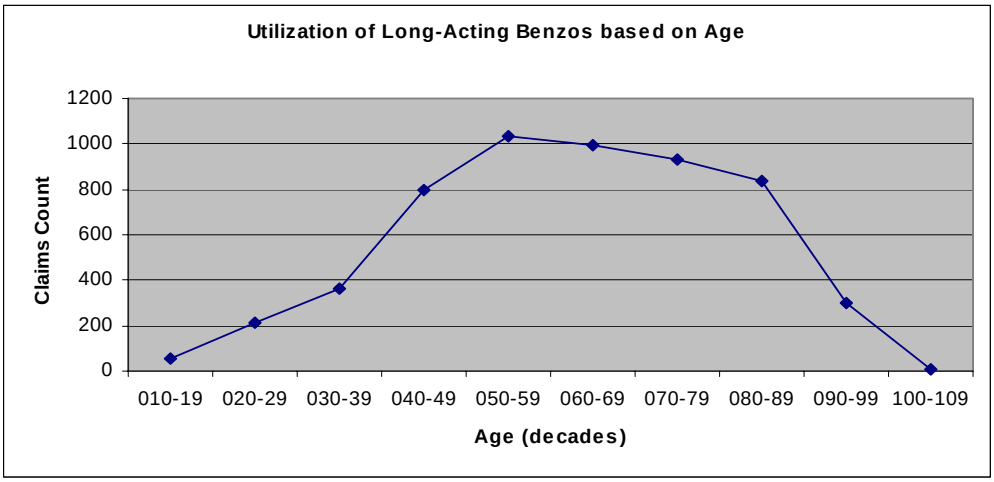


5) For beneficiaries who are receiving benzodiazepines, how many are also taking a maintenance medication for anxiety-related disorders in conjunction with the benzodiazepine?

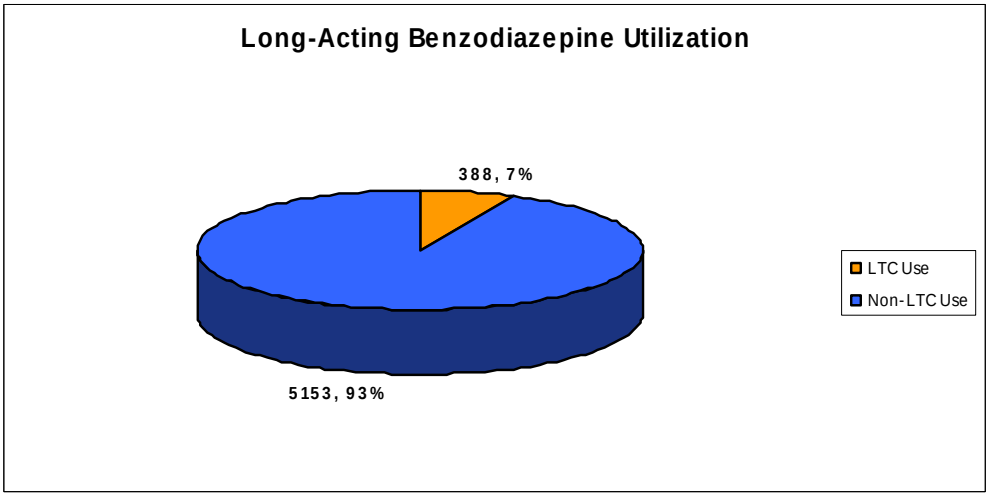


Of the benzodiazepines researched in this analysis, clonazepam had the largest percentage of users who were also taking an SSRI or Effexor XR® at 25%, followed closely by alprazolam. Lorazepam and diazepam had the lowest number of patients concurrently receiving maintenance therapy with an SSRI or Effexor XR®, at 14%.

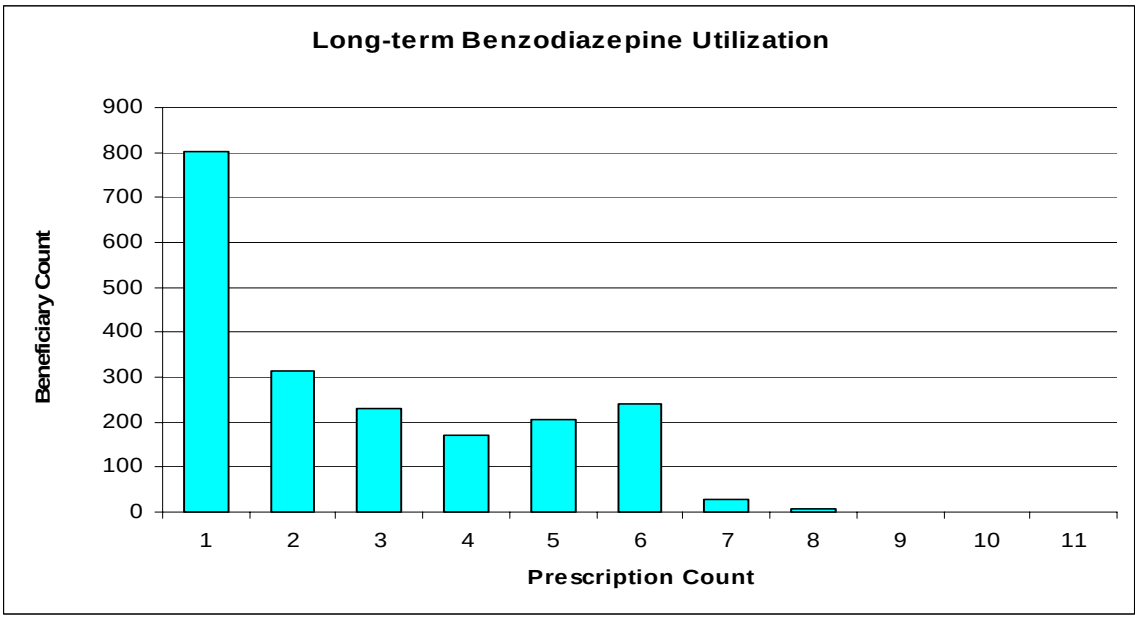
6) **What are the utilization trends for the long-acting benzodiazepines (flurazepam, triazolam, estazolam, and temazepam)?**



Use of the long-acting benzodiazepines peaks in the 50-59 age group, and slowly declines throughout the 60-89 age range, falling off sharply after this point. As mentioned before, the incidence of insomnia increases with age, so this is not a startling discovery.

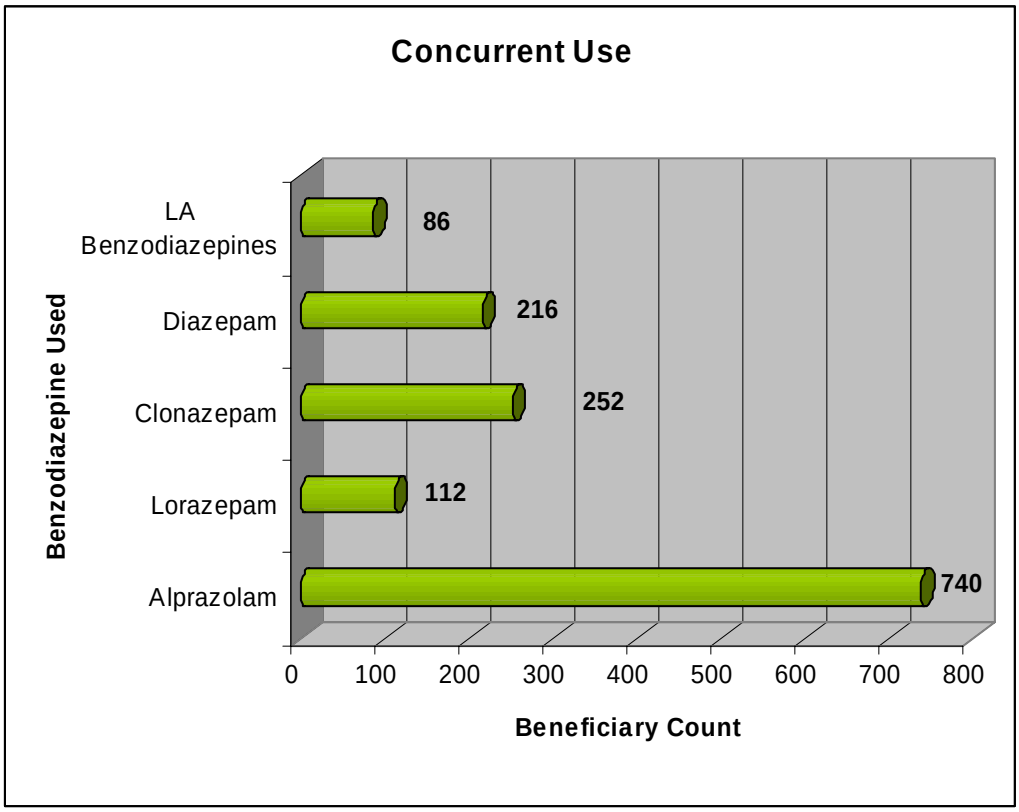


Of the utilization of long-acting benzodiazepines, only 7% of the use of these medications occurs in the traditional long-term care population. This is an encouraging finding, considering that these particular benzodiazepines are considered to be more dangerous for the LTC population with the long-half lives and increased sedation associated with them. These properties can increase the risk of falls and other incidents in an already frail population.



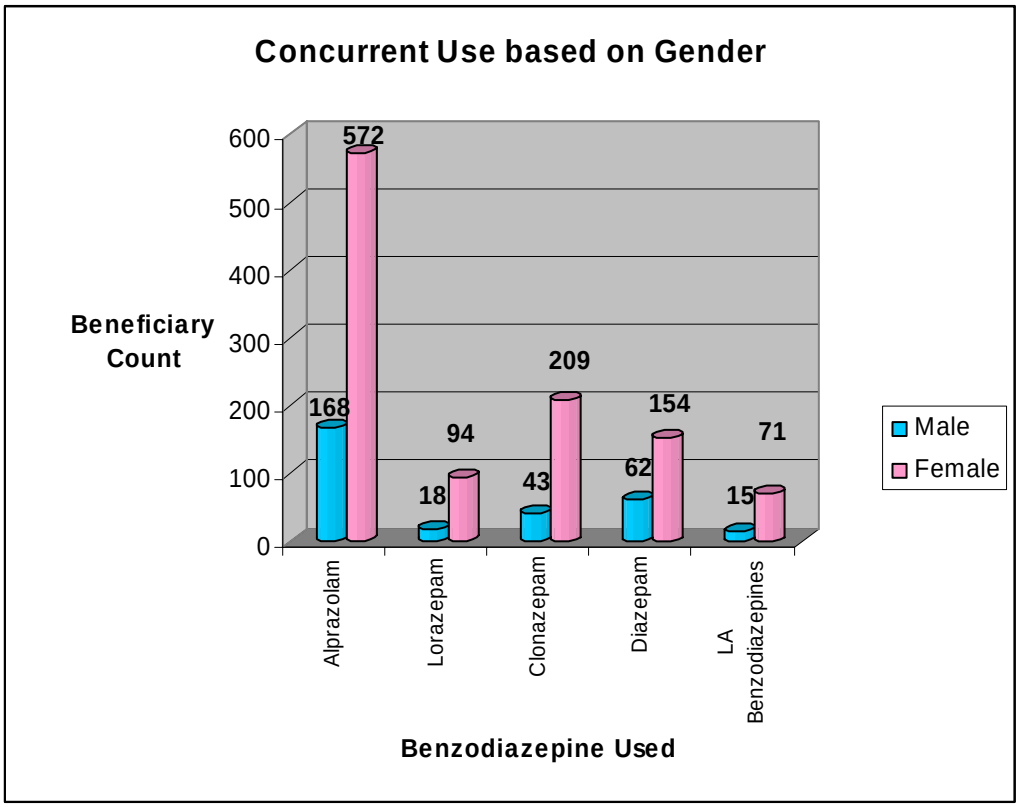
The majority of beneficiaries who received a prescription for a long-acting benzodiazepine did so only once, which represented approximately 800 beneficiaries. A much smaller number received between 2 and 6 prescriptions, with almost none receiving more than 6 prescriptions for a long-acting benzodiazepine.

7) What is the incidence of beneficiaries receiving a combination of a benzodiazepine, hydrocodone, and carisoprodol?



The prevalence of concurrent use of these medications varies greatly with the benzodiazepine used. For those beneficiaries taking alprazolam, a much larger number of these patients also received hydrocodone and carisoprodol during the same time frame. However, for those patients taking lorazepam or the long-acting benzodiazepines, the concurrent use with hydrocodone and carisoprodol during the same time period was much less.

As the chart below shows, the females by far are the most common users of all 3 medications concomitantly. For diazepam, the use with hydrocodone and carisoprodol in females is at least double that of males. In the case of alprazolam, females outnumber males 3 to 1 when looking at the use of all 3 medications concurrently. For clonazepam, lorazepam, and long-acting benzodiazepines, female use of hydrocodone and carisoprodol along with the respective benzodiazepine is almost 5 times that of males.


Concurrent Use based on Gender
Beneficiary Count
600
500
400
300
200
100
0
572
168
94
18
209
43
154
62
71
15
Alprazolam
Lorazepam
Clonazepam
Diazepam
LA Benzodiazepines
Benzodiazepine Used
Male
Female

Labeling Update for Desmopressin Acetate Nasal Spray

Introduction

Primary nocturnal enuresis (PNE) is a disorder characterized as 1 to 2 bed-wetting incidents a week over a 3 month period in children over the age of 5, and is most commonly seen in boys. There are several causes of PNE, including delayed growth, a small bladder, too little antidiuretic hormone, deep sleeping, or emotional/social factors such as stress. By the age of 15, most children who experience this problem have learned bladder control and no longer experience bed-wetting episodes. Treatment of this syndrome can include alarm devices, behavior therapy, and pharmacological treatment options.

Problem

On December 4, 2007, the FDA required manufacturers of desmopressin to update prescribing information for their products to include important new safety information about severe hyponatremia and seizures. Certain patients, including children treated with the intranasal formulation of desmopressin for PNE, are at risk for developing severe hyponatremia that can result in seizures and death. As such, desmopressin intranasal formulations are no longer indicated for the treatment of primary nocturnal enuresis and should not be used in hyponatremic patients or patients with a history of hyponatremia. The following chart lists the medications affected by this change.

Drug Name
Desmopressin Acetate Nasal Spray Pump
DDAVP® Nasal Spray Pump and Rhinal Tube Deliver System
Stimate® Nasal Spray
Minirin® Nasal Spray

Method

Utilization data was gathered through RxExplorer®, which searches through paid claims data submitted to HID by the fiscal agent. A search was conducted covering the period from 1/1/2007 through 11/23/2007, which was the most recent date for which data was available.

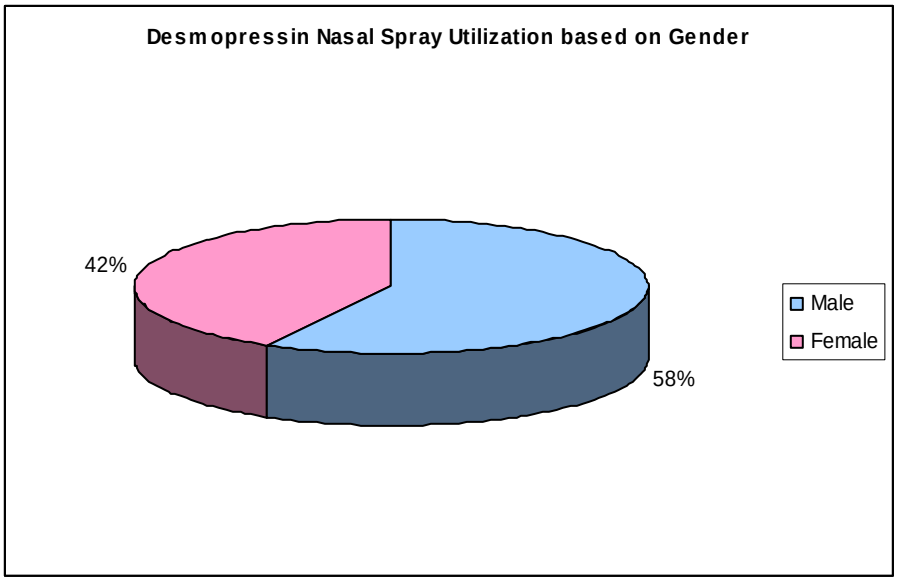
The search parameters were desmopressin nasal spray utilization for children ages 5 to 15. The search was then analyzed to determine the current utilization of this medication and delivery system in this population.

Results

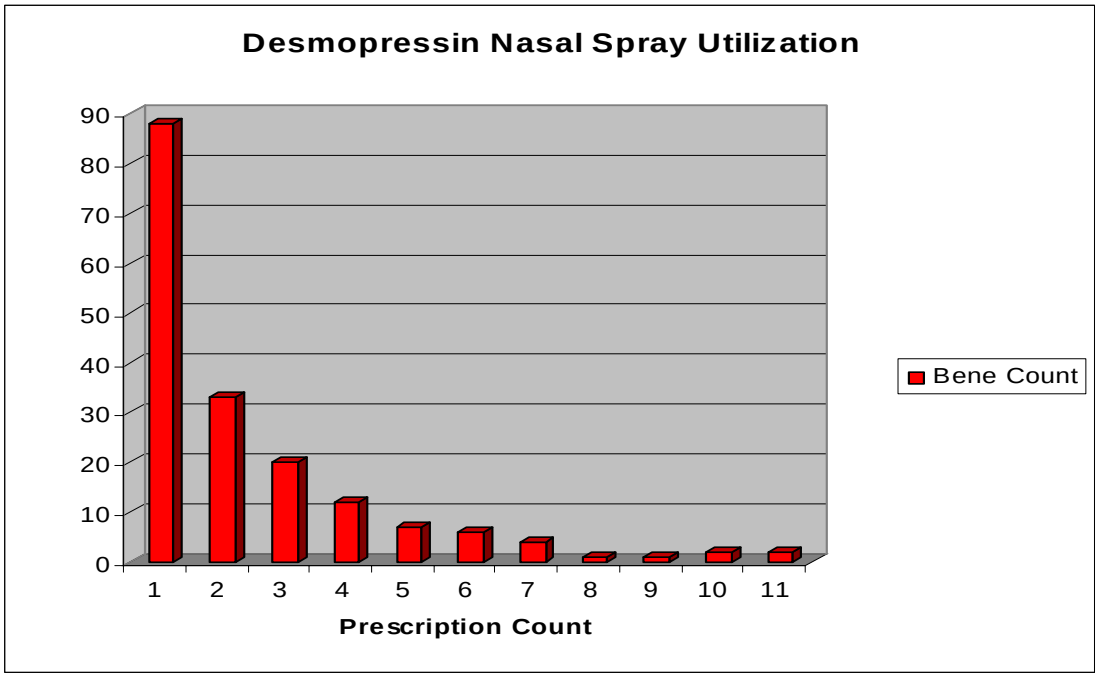
During the time period from January 1, 2007 to November 23, 2007, there were a total of 420 claims for desmopressin acetate nasal spray in children ages 5 to 15, representing a total of 176 beneficiaries. Of these 176 children, 89 (51%) had a diagnosis of either enuresis or nocturnal enuresis.

Drug Name	Rx Count
Desmopressin 0.1mg/mL Spray	417
Stimate® 1.5mg/mL Nasal Spray	3
Total	**420**

74 females and 102 males received desmopressin nasal spray during this time frame, which is consistent with the normal gender trend for PNE.



Of those beneficiaries who received desmopressin nasal spray, the largest percentage of them received between 1 and 3 prescriptions, with very few receiving long-term treatment with this medication.



Summary

Based on the information gathered in this data search, there is not extensive utilization of desmopressin nasal spray in children ages 5 to 15 in the Mississippi Medicaid population. Of those beneficiaries receiving this medication, a very small number receive long-term treatment with desmopressin nasal spray.

Recommendations

While the overall percentage of beneficiaries receiving desmopressin nasal spray is not great, the serious nature of the problems experienced with this medication warrant prudent use of desmopressin nasal spray. Retrospective DUR criteria are recommended to identify those patients who may be receiving this medication in violation of the recent position of the FDA.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
Desmopressin-related Criteria
February 2008

Criteria Recommendations ***Accepted*** ***Rejected***

1. Desmopressin / Therapeutic Appropriateness _____ _____

Alert Message: Desmopressin may cause severe hyponatremia which may put patients at risk for seizures and death. Intranasal desmopressin is no longer indicated for the treatment of primary nocturnal enuresis (PNE). The agent should not be used in patients with hyponatremia or a history of hyponatremia. Desmopressin tablets are still indicted for the treatment of PNE but therapy should be interrupted during acute illness that may lead to fluid or electrolyte imbalance.

Conflict Code: TA - Therapeutic Appropriateness

Drugs/Diseases

Util A	Util B	Util C
Desmopressin		

References:

MedWatch - The FDA Safety Information and Adverse Event Reporting Program, 2007.
DDAVP Prescribing Information, October 2007, Sanofi-Aventis.

2. Desmopressin / Pressor Agents _____ _____

Alert Message: The concomitant administration of drugs that may increase the risk of water intoxication with hyponatremia (e.g., tricyclic antidepressants, selective serotonin re-uptake inhibitors, chlorpromazine, opiate analgesics, NSAIDS, lamotrigine, and carbamazepine) should be performed with caution.

Conflict Code: DD – Drug/Drug Interaction

Drugs/Diseases

Util A	Util B	Util C
Desmopressin	Tricyclic Antidepressants	
	Selective Serotonin Re-uptake Inhibitors	
	Chlorpromazine	
	Opiate Analgesics	
	NSAIDS	
	Lamotrigine	
	Carbamazepine	

References:

DDAVP Prescribing Information, October 2007, Sanofi-Aventis.
Facts & Comparisons, 2007 Updates.

Pharmacy Coverage of Tobacco Cessation Products

As a result of a recent federal directive, states were instructed to strengthen their efforts to encourage and support smoking cessation in multiple areas, including pharmacy coverage. Beginning 11/1/07, Mississippi Medicaid broadened its coverage of tobacco cessation products to include the new agent Chantix®. Previously, nicotine replacement products and bupropion sustained-release tablets were the only covered products for smoking cessation.

Chantix® (varenicline) binds with high affinity and selectivity to neuronal nicotinic acetylcholine receptors. The efficacy of Chantix® in smoking cessation is believed to be the result of its binding to these receptors, which produces agonist activity while simultaneously preventing nicotine binding to the same receptors. Electrophysiology studies in vitro have shown that Chantix® binds to α4β2 neuronal nicotinic acetylcholine receptors and stimulates receptor-mediated activity, but at a significantly lower level than nicotine. Chantix® blocks the ability of nicotine to activate α4β2 receptors and, thus, to stimulate the central nervous mesolimbic dopamine system, believed to be the neuronal mechanism underlying reinforcement and reward experienced upon smoking.

The chart below illustrates the utilization of all the tobacco cessation products from 11/01/07 (the beginning date of coverage for Chantix®) to 12/21/07 (the most recent date for which claims data was available).

Prescription Count	Total Beneficiaries - Chantix®	Total Beneficiaries - Nicotine Patch/Gum/Lozenge
1	338	59
2	53	8
3	1	2
4	0	1
6	0	1
Totals	**392**	**71**

Based on the information above, the coverage of Chantix® by Mississippi Medicaid has provided many beneficiaries with another tool to help in their endeavors to stop smoking. From 2006, the number of beneficiaries who sought pharmacological help to quit smoking increased from 102 to 463. This increase most likely can be attributed to the coverage of Chantix®. The utilization of Chantix® was approximately 5 times that of the nicotine replacement products, with nearly 15% of beneficiaries receiving a second prescription of either agent to continue in their efforts.

With the treatment of tobacco-related illness costing Mississippi Medicaid roughly **$264 million** each year, any attempt to reduce the use of tobacco products by Medicaid beneficiaries is a positive one. Mississippi Medicaid has made a step in the right direction to potentially lower health-care costs in the future by providing another option to support those beneficiaries who are making the effort to stop smoking.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
FEBRUARY 2008

Criteria Recommendations	*Accepted*	*Rejected*

1. Nebivolol / High Dose _____ _____

Alert Message: Bystolic (nebivolol) may be over-utilized. The recommended maximum dose is 40 mg per day.
Conflict Code: HD – High Dose
Drugs/Disease

Util A	Util B	Util C
Nebivolol		

Max Dose: 40 mg/day
References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

2. Nebivolol / Contraindications _____ _____

Alert Message: Bystolic (nebivolol) is contraindicated in patients with severe bradycardia, heart block greater than first degree, cardiogenic shock, decompensated cardiac failure, sick sinus syndrome (no permanent pacemaker in place), hypersensitivity to the product, or severe hepatic impairment (Child-Pugh >B).
Conflict Code: MC – Drug Actual Disease Problem
Drugs/Disease

Util A	Util B	Util C
Nebivolol	Bradycardia	
	Heart Block	
	Cardiogenic Shock	
	Cardiac failure	
	Sick Sinus Syndrome	

References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

3. Nebivolol / Hepatic Impairment _____ _____

Alert Message: Bystolic (nebivolol) is contraindicated in patients with severe hepatic impairment and should be used with caution in patients with moderate impairment. Studies have shown patients with moderate hepatic impairment have an 86% decrease in nebivolol clearance. The recommended initial dose of nebivolol in patients with moderate impairment is 2.5 mg once daily with upward titration performed cautiously if needed.
Conflict Code: DB – Drug/Drug or Drug Disease Precaution
Drugs/Disease

Util A	Util B	Util C
Nebivolol	Hepatic Impairment	

References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

Criteria Recommendations *Accepted* *Rejected*

4. Nebivolol / Renal Impairment _____ _____

Alert Message: Bystolic (nebivolol) should be used with caution in patient with severe renal impairment. Studies have shown a 53% decrease in the renal clearance of nebivolol in patients with a CrCl < 30 mL/min. The recommended initial dose of nebivolol in this population is 2.5 mg once daily with upward titration performed cautiously if needed.
Conflict Code: DB – Drug/Drug or Drug Disease Precaution
Drugs/Disease

Util A	Util B	Util C
Nebivolol	Severe Renal Impairment	
	Lanthanum	
	Sevelamer	
	Doxercalciferol	
	Paricalcitol	
	Calcitriol	

References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

5. Nebivolol / CYP2D6 Inhibitors _____ _____

Alert Message: The concurrent administration of Bystolic (nebivolol) and a CYP2D6 inhibitor (e.g., paroxetine, fluoxetine, quinidine, and bupropion) is expected to result in elevated nebivolol plasma concentrations. Patients receiving concurrent therapy with these agents should be monitored closely and the nebivolol dose adjusted according to blood pressure response.
Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease

Util A	Util B	Util C
Nebivolol	Paroxetine	
	Fluoxetine	
	Quinidine	
	Bupropion	
	Duloxetine	
	Amiodarone	
	Cimetidine	
	Propafenone	

References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

6. Nebivolol / CYP2D6 Inducers _____ _____

Alert Message: The concurrent administration of Bystolic (nebivolol) and a CYP2D6 inducer (e.g., rifampin and dexamethasone) is expected to result in decreased nebivolol plasma concentrations. Patients receiving concurrent therapy with these agents should be monitored closely and the nebivolol dose adjusted according to blood pressure response.
Conflict Code: DD – Drug/Drug Interactions
Drugs/Disease

Util A	Util B	Util C
Nebivolol	Dexamethasone	
	Rifampin	

References:
Bystolic Prescribing Information, December 2007, Forest Pharmaceuticals, Inc.

Criteria Recommendations *Accepted* *Rejected*

7. Atypical Antipsychotics / Therapeutic Duplication _____ _____

Alert Message: Therapeutic duplication of atypical antipsychotic agents may be occurring.
Conflict Code: TD – Therapeutic Duplication
Drugs/Disease

Util A	Util B	Util C
Clozapine		
Risperidone		
Olanzapine		
Quetiapine		
Ziprasidone		
Aripiprazole		
Paliperidone		

References:
Facts & Comparisons, 2007 Updates.
Clinical Pharmacology, Gold Standard, 2007.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2007.

8. Risperdal Consta / Oral Atypical Antipsychotics _____ _____

Alert Message: Patients prescribed Risperdal Consta (risperidone injection) should receive oral antipsychotic supplementation until risperidone has achieved steady-state plasma concentrations, typically after 4 injections. The use of oral antipsychotics with risperidone injection beyond the recommended transition time period may represent an unnecessary and costly duplication of therapy.
Conflict Code: TD – Therapeutic Duplication (DD-100P)
Drugs/Disease

Util A	Util B	Util C
Risperdal Consta	Clozapine	
	Risperidone (except Consta)	
	Olanzapine	
	Quetiapine	
	Ziprasidone	
	Aripiprazole	
	Paliperidone	

References:
Risperdal Consta Prescribing Information, Sept 2007, Janssen Pharmaceuticals, Ltd.
Facts & Comparisons, 2007 Updates.
Clinical Pharmacology, Gold Standard, 2007.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2007.

Boxed Warning Update

The following information is provided to the DUR Board to assist in identifying drug products with potential for concern surrounding safety and appropriate utilization. Most of the safety alert information provided is derived from recent FDA safety alerts. While many of the alerts included are not Black Box Warning additions or updates, they are labeling changes or updates with relevance worthy of action by FDA.

Included for reference, the following is the Code of Federal Regulations definition for Black Box Warnings. (Citation: Title 21 CFR 201.57 Section E)

(e) Warnings. Under this section heading, the labeling shall describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and steps that should be taken if they occur. The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved. A specific warning relating to a use not provided for under the "Indications and Usage: section of labeling may be required by the Food and Drug Administration if the drug is commonly prescribed for a disease of condition, and there is lack of substantial evidence of effectiveness for that disease or condition, and such usage is associated with serious risk or hazard. Special problems, particularly those that may lead to death or serious risk or hazard. Special problems, particularly those that may lead to death or serious injury, may be required by the Food and Drug Administration to be placed in a prominently displayed box. The boxed warning ordinarily shall be based on clinical data, but serious animal toxicity may also be the basis of a boxed warning in the absence of clinical data. If a boxed warning is required, its location will be specified by the Food and Drug Administration. The frequency of these adverse reactions and , if known, the approximate mortality and morbidity rates for patients sustaining the reaction, which are important to safe and effective used of the drug, shall be expressed as provided under the "Adverse Reactions" section of the labeling.

Ortho Evra Contraceptive Transdermal Patch

1/19/2008: FDA modified the prescribing information for the Ortho Evra Contraceptive Transdermal (Skin) Patch to include the results of a new epidemiology study that found that users of the birth control patch were at higher risk of developing serious blood clots, also known as venous thromboembolism (VTE), than women using birth control pills. VTE can lead to pulmonary embolism. The label changes are based on a study conducted by the Boston Collaborative Drug Surveillance Program on behalf of Johnson and Johnson. The patch was studied in women aged 15-44. These findings support an earlier study that also said women in this group were at higher risk for VTE.

FDA believes that Ortho Evra is a safe and effective method of contraception when used according to the labeling, which recommends that women with concerns or risk factors for serious blood clots talk with their health care provider about using Ortho Evra versus other contraceptive options.

Cough and Cold Medications in Children Less Than Two Years of Age
1/17/2008: FDA informed consumers and healthcare professionals that the Agency has completed its review of information regarding the safety of over-the-counter (OTC) cough and cold medicines in children under 2 years of age and recommends that these drugs not be used to treat children in this age group because serious and potentially life-threatening side effects can occur. FDA's recommendation is based on both the review of the information the Agency received about serious side effects in children in the referenced age group and the discussion and recommendations made at the October 18 - 19, 2007, public advisory committee meeting at which this issue was discussed. FDA has not completed its review of information about the safety of OTC cough and cold medicines in children 2 through 11 years of age. See the FDA Public Health Advisory for Agency recommendations regarding this issue.

Edetate Disodium (marketed as Endrate and generic products)
1/16/2008: FDA notified healthcare professionals and patients about important safety information concerning Edetate Disodium. There have been cases where children and adults have died when they were mistakenly given Edetate Disodium instead of Edetate Calcium Disodium (Calcium Disodium Versenate) or when Edetate Disodium was used for "chelation therapies" and other uses that are not approved by the FDA. Edetate Disodium was approved as an emergency treatment for certain patients with hypercalcemia (very high levels of calcium in the blood) or certain patients with heart rhythm problems as a result of very high amounts of digitalis in the blood. Edetate Calcium Disodium was approved to reduce dangerously high blood lead levels (severe lead poisoning).

The two drugs have very similar names and are commonly referred to only as EDTA. As a result, the two products are easily mistaken for each other when prescribing, dispensing, and administering them. Edetate Disodium and Edetate Calcium Disodium works by binding with heavy metals or minerals in the body allowing them to be passed out of the body through the urine. Read the FDA Public Health Advisory for recommended and important safety considerations for healthcare professionals until the FDA's ongoing evaluation of the risks and benefits of Edetate Disodium is complete.

Compounded Menopause Hormone Therapy Drugs
1/10/2008: FDA informed healthcare professionals and patients that the Agency sent letters warning seven pharmacy operations that the claims they make about the safety and effectiveness of their so-called "bio-identical hormone replacement therapy," or "BHRT" products are unsupported by medical evidence, and are considered false and misleading by the agency. The pharmacy operations improperly claim that their drugs, which contain hormones such as estrogen, progesterone, and estriol (which is not a component of an FDA-approved drug and has not been proven safe and effective for any use) are superior to FDA-approved menopausal hormone therapy drugs and prevent or treat serious diseases, including Alzheimer's disease, stroke, and various forms of cancer. FDA is concerned that the claims for safety, effectiveness, and superiority that these pharmacy operations are making mislead patients, as well as doctors and other healthcare

professionals. Compounded drugs are not reviewed by the FDA for safety and effectiveness.

Patients who use compounded hormone therapy drugs should discuss menopausal hormone therapy options with their healthcare provider to determine if compounded drugs are the best option for their specific medical needs.

Bisphosphonates (marketed as Actonel, Actonel+Ca, Aredia, Boniva, Didronel, Fosamax, Fosamax+D, Reclast, Skelid, and Zometa)
1/07/2008: FDA informed healthcare professionals and patients of the possibility of severe and sometimes incapacitating bone, joint, and/or muscle (musculoskeletal) pain in patients taking bisphosphonates. Although severe musculoskeletal pain is included in the prescribing information for all bisphosphonates, the association between bisphosphonates and severe musculoskeletal pain may be overlooked by healthcare professionals, delaying diagnosis, prolonging pain and/or impairment, and necessitating the use of analgesics. The severe musculoskeletal pain may occur within days, months, or years after starting a bisphosphonates. Some patients have reported complete relief of symptoms after discontinuing the bisphosphonate, whereas others have reported slow or incomplete resolution. The risk factors for and incidence of severe musculoskeletal pain associated with bisphosphonates are unknown.

Fentanyl Transdermal System (marketed as Duragesic and generics)
12/21/2007: FDA issued an update that highlights important information on appropriate prescribing, dose selection, and the safe use of the fentanyl transdermal system (patch). FDA previously issued a Public Health Advisory and Information for Healthcare Professionals in July 2005 regarding the appropriate and safe use of the transdermal system. However, the Agency continues to receive reports of death and life-threatening adverse events related to fentanyl overdose that have occurred when the fentanyl patch was used to treat pain in opioid-naive patients and when opioid-tolerant patients have applied more patches than prescribed, changed the patch too frequently, and exposed the patch to a heat source. The fentanyl patch is only indicated for use in patients with persistent, moderate to severe chronic pain who have been taking a regular, daily, around-the-clock narcotic pain medicine for longer than a week and are considered to be opioid-tolerant.

Patients must avoid exposing the patch to excessive heat as this promotes the release of fentanyl from the patch and increases the absorption of fentanyl through the skin which can result in fatal overdose. Directions for prescribing and using the fentanyl patch must be followed exactly to prevent death or other serious side effects from fentanyl overdose.

Carbamazepine (marketed as Carbatrol, Equetro, Tegretol and generics)
12/12/2007: FDA informed healthcare professionals that dangerous or even fatal skin reactions (Stevens Johnson syndrome and toxic epidermal necrolysis), that can be caused by carbamazepine therapy, are significantly more common in patients with a particular human leukocyte antigen (HLA) allele, HLA-B*1502. This allele occurs almost exclusively in patients with ancestry across broad areas of Asia, including South Asian

Indians. Patients with ancestry from areas in which HLA-B*1502 is present should be screened for the HLA-B*1502 allele before starting treatment with carbamazepine. If these individuals test positive, carbamazepine should not be started unless the expected benefit clearly outweighs the increased risk of serious skin reactions. Patients who have been taking carbamazepine for more than a few months without developing skin reactions are at low risk of these events ever developing from carbamazepine. This is true for patients of any ethnicity or genotype, including patients positive for HLA-B*1502.

Desmopressin Acetate (marketed as DDAVP Nasal Spray, DDAVP Rhinal Tube, DDAVP, DDVP, Minirin, and Stimate Nasal Spray)
12/04/2007: FDA notified healthcare professionals and patients of the Agency's request that manufacturers update the prescribing information for desmopressin to include important new safety information about severe hyponatremia and seizures. Certain patients, including children treated with the intranasal formulation of the drug for primary nocturnal enuresis (PNE), are at risk for developing severe hyponatremia that can result in seizures and death. As such, desmopressin intranasal formulations are no longer indicated for the treatment of primary nocturnal enuresis and should not be used in hyponatremic patients or patients with a history of hyponatremia. PNE treatment with desmopressin tablets should be interrupted during acute illnesses that may lead to fluid and/or electrolyte imbalance. All desmopressin formulations should be used cautiously in patients at risk for water intoxication with hyponatremia.

Chantix (Varenicline)
11/20/2007: FDA informed healthcare professionals of reports of suicidal thoughts and aggressive and erratic behavior in patient who have taken Chantix, a smoking cessation product. There are also reports of patients experiencing drowsiness that affected their ability to drive or operate machinery. FDA is currently reviewing these cases, along with other recent reports. A preliminary assessment reveals that many of the cases reflect new-onset of depressed mood, suicidal ideation, and changes in emotion and behavior within days to weeks of initiating Chantix treatment. The role of Chantix in these cases is not clear because smoking cessation, with or without treatment, is associated with nicotine withdrawal symptoms and has also been associated with the exacerbation of underlying psychiatric illness. However, not all patients described in the cases had preexisting psychiatric illness and not all had discontinued smoking.

Healthcare professionals should monitor patients taking Chantix for behavior and mood changes. Patients taking this product should report behavior or mood changes to their doctor and use caution when driving or operating machinery until they know how quitting smoking with Chantix may affect them.

Erythropoiesis Stimulating Agents: Aranesp (darbepoetin alfa), Epogen (epoetin alfa), and Procrit (epoetin alfa)
Updated 1/03/2008: FDA informed healthcare professionals of findings from two additional clinical studies, Preoperative Epirubicin Paclitaxel Aranesp Study (PREPARE), and the National Cancer Institute Gynecologic Oncology Group (COG-19), showing an increase in mortality and shorter time to tumor progression in patients with

cancer receiving an Erythropoiesis-Stimulating Agent (ESA). Both the PREPARE study in breast cancer and the COG-19 study in cervical cancer showed higher rates of death and or tumor progression in patients who received an ESA compared to patients who did not receive an ESA. FDA strongly recommends that healthcare professionals discuss the risks of ESA-associated tumor progression and shortened survival in patients with cancer before starting or continuing ESA therapy.

Posted 11/08/2007: FDA notified healthcare professionals of revised boxed warnings and other safety-related product labeling changes for erythropoiesis-stimulating agents (ESAs), which treat certain types of anemia. These new statements address the risks that the drugs Aranesp, Epogen, and Procrit pose to patients with cancer and patients with chronic kidney failure. For patients with cancer, the new boxed warnings emphasize that ESAs caused tumor growth and shortened survival in patients with advanced breast, head and neck, lymphoid and non-small cell lung cancer when they received a dose that attempted to achieve a hemoglobin level of 12 grams per deciliter (g/dL) or greater. For patients with chronic kidney failure, the new boxed warning states that ESAs should be used to maintain a hemoglobin level between 10 g/dL to 12 g/dL. Maintaining higher hemoglobin levels in patients with chronic kidney failure increases the risk of death and other serious conditions. The new labeling provides specific instructions for dosage adjustments and hemoglobin monitoring for chronic kidney failure patients who do not respond to ESA treatment with an adequate increase in their hemoglobin levels. Additionally, the new boxed warnings clarify that ESAs should only be used in patients with cancer when treating anemia specifically caused by chemotherapy and not for other causes of anemia. Further, it states that ESAs should be discontinued once the patient's chemotherapy course has been completed.

CellCept (mycophenolate mofetil)
Updated 11/27/2007: Prescribing information for Mycophenolic Acid (marketed as Myfortic Delayed Released Tablets) revised to include information that use of drug during pregnancy is associated with increased risks of pregnancy loss and congenital malformations. See the MedWatch alert for Myfortic (mycophenolic acid).

[Posted 10/29/2007] Roche and FDA notified healthcare providers that use of CellCept (mycophenolate mofetil) is associated with increased risk of first trimester pregnancy loss and increased risk of congenital malformations, especially external ear and facial abnormalities including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney. Based on postmarketing data from the United States National Transplantation Pregnancy Registry and additional postmarketing data collected in women exposed to systemic mycophenolate mofetil during pregnancy, the pregnancy category for CellCept has been changed from Category C (risk of fetal harm cannot be ruled out) to Category D (positive evidence of fetal risk). Labeling changes include the following sections: BOXED WARNING, WARNINGS/Pregnancy and Pregnancy Exposure Prevention, PRECAUTIONS/Information for Patients, and ADVERSE REACTIONS/Postmarketing Experience.

Within one week of beginning CellCept therapy, women of childbearing potential should have a negative serum or urine pregnancy test. In addition, women of childbearing potential (including pubertal girls and peri-menopausal woman) taking CellCept must receive contraceptive counseling and use effective contraception. Healthcare professionals and patients should be aware that CellCept reduces blood levels of the hormones in the oral contraceptive pill and could theoretically reduce its effectiveness. See the Dear Healthcare Professional Letter for additional recommendations for women of childbearing potential.

Provigil (modafinil) Tablets
10/24/2007: FDA and Cephalon notified healthcare professionals of updates to the WARNINGS section of the prescribing information for Provigil (modafinil). Provigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder. The revised labeling updates safety information to include warnings regarding serious rash, including Stevens-Johnson Syndrome (SJS) and hypersensitivity reactions, and psychiatric symptoms. Rare cases of serious or life-threatening rash, including Toxic Epidermal Necrolysis, and Drug Rash with Eosinophilia and Systemic Symptoms have been reported in adults and children in worldwide postmarketing experience. Angioedema and multi-organ hypersensitivity reactions have also been reported in postmarketing experience.

Physicians should instruct their patients to immediately discontinue the use of Provigil and contact them if a rash or other hypersensitivity reaction occurs. Healthcare professionals and consumers should also be aware that Provigil is not approved for use in pediatric patients for any indication. In addition, psychiatric adverse experiences (including anxiety, mania, hallucinations, and suicidal ideation) have been reported in patients treated with Provigil. Caution should be exercised when Provigil is given to patients with a history of psychosis, depression, or mania.

Additional labeling revisions were made to the CLINICAL PHARMACOLOGY, PRECAUTIONS, and PATIENT PACKAGE INSERT sections. See revised labeling below.

Viagra (sildenafil), Cialis (tadalafil), Levitra (vardenafil), Revatio (sildenafil)
10/18/2007: FDA informed healthcare professionals of reports of sudden decreases or loss of hearing following the use of PDE5 inhibitors Viagra, Levitra, Cialis for the treatment of erectile dysfunction, and Revatio for the treatment of pulmonary arterial hypertension. In some cases, the sudden hearing loss was accompanied by tinnitus and dizziness. Medical follow-up on these reports was often limited which makes it difficult to determine if the loss of hearing was related to the use of one of the drugs, an underlying medical condition or other risk factors for hearing loss, a combination of these factors or other factors. The PRECAUTIONS and ADVERSE REACTIONS sections of the approved product labeling for Viagra, Levitra, and Cialis were revised. FDA is working with the manufacturer to revise the labeling for Revatio.

Byetta (exenatide)
10/16/2007: FDA has reviewed 30 postmarketing reports of acute pancreatitis in patients taking Byetta (exenatide), a drug used to treat adults with type 2 diabetes. An association between Byetta and acute pancreatitis is suspected in some of these cases. Amylin Pharmaceuticals, Inc. has agreed to include information about acute pancreatitis in the PRECAUTIONS section of the product label.

Healthcare professionals should be alert to the signs and symptoms of acute pancreatitis and instruct patients taking Byetta to seek prompt medical care if they experience unexplained, persistent, severe abdominal pain which may or may not be accompanied by vomiting. If pancreatitis is suspected, Byetta should be discontinued. If pancreatitis is confirmed, Byetta should not be restarted unless an alternative etiology is identified.